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FOCAL EPILEPSY

A Statistical Study of Its Causes and the Results of Surgical Treatment

II. Epilepsy Secondary to Cerebral Trauma and Infection*

JAMES C. WHITE, M.D.,† CHING TUNG LIU, M.D.,‡ AND WILLIAM JASON MIXTER, M.D.§

BOSTON

THIS is the second of two papers reviewing surgical experience with 240 epileptic patients at the Massachusetts General Hospital in the decade 1935 through 1944. These patients in whom the epileptogenic focus could be localized clinically and visualized at operation therefore amount to 21 per cent of the total 1130 hospital admissions for epilepsy. In the preceding paper the relation of seizures to tumor of the brain was discussed.[1] Tumors are the most important etiologic factor in this group of epileptic patients with a local operable condition, since approximately a third of those in whom such lesions were situated above the tentorium had convulsions. One hundred and sixty tumors made up two thirds of the total operable cases. This paper considers the role of cerebral trauma and infection, with material based on 80 patients.

The modern surgical attack on epilepsy due to focal injury of the brain dates back to the pioneer work of Professor Otfrid Foerster[2] on gunshot injuries of the brain in German soldiers of World War I. Penfield, who studied with him in Breslau in 1927, has made the greatest advances and written the outstanding monograph on the subject with Erickson, describing the technic and results in the extensive series of cases from the Neurological Institute in Montreal.[3] As pointed out in the preceding paper, special interest began to be focused on this group of patients with focal epileptogenic lesions¶ at the Massachusetts General Hospital in 1935. Air studies, either by pneumoencephalography or by ventriculography, have been carried out routinely throughout this period, and electroencephalography since 1937. Penfield's method of mapping the cerebral cortex of the patient under local anesthesia with the thyratron stimulator has been used in these operations. In the last year of World War II the development of a cortical electrode holder and of the technic for "activated electroencephalography" on Dr. A. Earl Walker's[4, 5] service at the Cushing General Hospital has provided a still more effective method of delimiting the area from which the epileptogenic discharge originates, but it is not safe to draw conclusions from such recent operations. We have therefore selected the decade 1935–1944 for statistical review because it gives a follow-up period from a minimum of two years up to a possible maximum of twelve for the evaluation of surgical results.

MATERIAL

Out of the total 80 patients submitted to exploration for seizures that were believed to have resulted from trauma or infection, 62 are available for statistical study of end results. These include 49 cases of acute or chronic seizures resulting from cerebral trauma and 13 following infection (Table 1). The remaining 18 cases were excluded for various reasons. Follow-up study was inadequate in 6. Three other patients turned out to have brain tumors (these cases are described below). In 7 with previously verified abscesses, 1 with cortical resection for athetosis and 1 with a subcortical hematoma following rupture of a cerebral aneurysm, operation for complicating mild seizures was not considered necessary. Epilepsy due to widespread cortical atrophy, diffuse degenerative disease, hydrocephalus and the hereditary forms of the disease is not suitable for surgical treatment, and failure to find operable lesions in some of the cases described below was due primarily to our lack of sufficient appreciation of this fact in the

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 25, 1948.

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¶Although the type of epilepsy observed in the great majority of these patients was the classic Jacksonian focal seizure, some had generalized attacks, and others only hallucinatory auras. The petit-mal form of epilepsy, however, rarely if ever starts from a superficial focus and is therefore not amenable to surgery.

earlier years of this decade. In some previous reports[3] the surgical epileptic cases have been subdivided on the pathological basis of expanding lesions and focal scars. In such a classification the intracranial hematomas and acute abscesses have been included with the neoplasms. In this review it has seemed best to discuss the actual tumors as a separate group.[1] We are therefore classifying the

TABLE 1. *Classification of Epilepsy after Cerebral Injury and Infection in 62 Patients Selected for Statistical Analysis.*

LESION		NO. OF CASES
Epidural hemorrhage (early or acute epilepsy)		5
Traumatic, from bleeding middle meningeal artery	1	
Postoperative bleeding	4	
Subdural hemorrhage (acute epilepsy)		10
Depressed and compound fractures (acute epilepsy)		6
Cerebral scars (chronic epilepsy)		28
Traumatic	27	
Postoperative	1	
Brain abscesses		13
Acute seizures	9	
Chronic seizures	4	
Total		62

hematomas with the post-traumatic group of depressed and compound fractures, meningocerebral cicatrices and focal cortical scars, and separating the abscesses into a third group of postinfectious cases (Table 1).

These two groups of post-traumatic and postinfectious cases, which are the subject of this paper, can be subdivided again on the basis of whether the lesion caused acute or chronic epilepsy. Thus the hematomas, depressed fractures and acute abscesses that may produce early seizures fall into the acute group, whereas healed abscesses and penetrating wounds of the brain that form contracting fibroglial scars may result in late chronic epilepsy.

EPILEPSY AFTER CEREBRAL TRAUMA

Acute Epilepsy from Cerebral Compression

Intracranial hematomas. Intracranial bleeding of all types may bring on convulsive seizures either by acute compression of the brain or by concomitant damage to the cortex.

Gamsu and Kubik,[6] who are making a special study of subarachnoid hemorrhage in this hospital, have found that bleeding of this type was accompanied by acute convulsions in 20 out of 118 cases. Fourteen patients died, with verification of ruptured congenital aneurysms in all 9 on whom postmortem examination was permitted. It deserves passing comment that only 2 of these brains on sectioning showed direct injury to the cortex and underlying white matter by intracerebral extension of the clot. In this decade these patients were not submitted to arteriography or ventriculography, and none had intracranial explorations. It is difficult to explain why acute seizures develop when hemorrhage is limited to the subarachnoid space. On the other hand, when blood burrows into the cortex and underlying white matter their occurrence is easy to understand, both in the acute stage and also at later periods if the patient survives and the clot is replaced by a meningocortical scar or deeper cerebral cicatrix. The situation here is identical with that seen after drainage and healing of cerebral abscesses, which are generally recognized as a cause of chronic seizures. At present we have a patient under observation in whom a large subcortical hematoma has been effectively evacuated and the bleeding point in the anterior cerebral artery ligated at another clinic.* Despite this brilliant diagnosis and life-saving surgical treatment, the delayed appearance of chronic epilepsy may necessitate another surgical intervention.

Focal seizures are a frequent warning signal of the development of a postoperative clot, having been present in 4 out of 12 cases that required secondary re-elevation of the bone flap for postoperative bleeding. These seizures are generally minor ones, producing fine twitching movements of the opposite side of the face, with rare extension to other areas. Prompt surgical exploration, with evacuation of the clot and control of any bleeding that is still present, has invariably resulted in early cessation of the seizures in both the postoperative hematomas and the post-traumatic variety discussed below.

Intracranial hematomas such as clots that occur after tearing of the middle meningeal artery may cause convulsive seizures. During this decade we have encountered this complication in only 1 of 9 cases of typical acute epidural hemorrhage following temporoparietal fractures with injury to the middle meningeal artery.

Subdural hematomas of venous origin, which expand much more slowly than the arterial extradural variety, may also lead to seizures. Kunkel and Dandy[7] reported attacks in 12.7 per cent of 48 cases, but Elvidge[8] concludes that this is a rare complication of subdural bleeding unless there is concomitant cortical injury. Our findings support those of Kunkel and Dandy.[7] Among 120 patients in whom such clots were diagnosed and evacuated, transitory seizures were observed in 10.† In 6 out of 7 cases in which there was no other obvious damage to the brain the seizures stopped and have not recurred. In the single exception there were only two attacks in the next two and a half years. In a case of closed head injury that had occurred eleven years previously, drainage of a large subdural hygroma has resulted in great improvement, so that the patient is able to

*This patient, a relative of one of us, was referred to Dr. J. L. Poppen.

†Three other subdural hematomas accompanied by convulsions have been drained during this decade. As it has been possible to keep the patients under observation for only a few months, their freedom from epilepsy cannot be regarded as permanent.

work despite occasional nocturnal seizures. In this patient circumscribed softening in the arm area was also present. A man who required evacuation of a subcortical clot in addition to a large subdural collection suffered mild sensory attacks every four to six months for two years, and has subsequently remained free for four years. Another, who in addition to a small subdural hematoma had a large subcortical clot with considerable contusion to the neighboring area of the brain, developed seizures for the first time six weeks after operation. In this case the chronic epilepsy, which has continued for the past two years, cannot be ascribed to the subdural hemorrhage, since an extensive cerebral cicatrix remains. Although subdural hematomas, if uncomplicated and evacuated early, are not likely to cause residual epilepsy, we have found trapped pockets of yellow fluid in the course of three operations for chronic epilepsy, which were probably residua of former extravasations of blood into the subdural space. One of these patients had had a hematoma evacuated one year previously.

Cortical compression from depressed fractures. Acute compression of the underlying cortex by simple depressed fractures of the cranial vault may lead to rapid onset of focal seizures. This was encountered in 6 of a series of 54 cases of these lesions. In each case there was definite cortical compression by the depressed cranial fragments, and the result of decompression by their elevation or removal was prompt and permanent disappearance of the seizures. This fortunate result is ascribed to the fact that in each of these civilian injuries the dura remained intact and the underlying cortex presumably was not lacerated, so that there was no permanent meningocerebral cicatrix or focal injury of the cortex to lead to late chronic epilepsy. Early removal of the compressing fragments, especially if in the vicinity of the motor cortex, is essential to prevent the formation of a cortical scar and a high incidence of chronic epilepsy. The following case report serves to illustrate this situation:

A 5-year-old girl riding her tricycle fell over an embankment and suffered a left temporoparietal depressed fracture (Fig. 1). She was briefly unconscious and then had a lucid interval. An hour later she again became comatose and developed twitching movements of the right side of the face and the right extremities. These soon became continuous, the coma deeper, and the respirations slow and labored. Exploration without anesthesia revealed a subgaleal hematoma and two large angulated fragments of bone, which deeply depressed the intact dura. As soon as these were elevated the convulsive movements ceased. There was no evidence of residual damage to the brain, and the patient left the hospital 10 days later in excellent condition. A recent follow-up letter, 5 years later, states that she is a nervous, maladjusted child at school, but has had no convulsive seizures.

Of the severer wartime injuries reported by Ascroft,[9] even when the dura was not torn, 23 per cent were followed by chronic seizures. This incidence, however, was only half as high as that when the dura was penetrated. When the underlying dura is torn and the cortex lacerated, especially in the presence of indriven fragments of bone or infection, even though the acute seizures may clear up, there is high incidence of chronic epilepsy. This amounted to 45 per cent in the best military statistics of World War I (Ascroft[9]), although indriven fragments were removed and damaged cortex radically sucked away. Injuries of this type are followed by scar formation and frequently result in recurrent seizures for this reason. It is a matter

FIGURE 1. *Comminuted Depressed Temporoparietal Fracture, Which Caused Acute Status Epilepticus.*

Continuous seizures ceased as soon as the depressed fragments were elevated.

of major concern to the United States Veterans Administration that there are listed 15,000 cases of craniocerebral injuries in which the patients have survived the present war, nearly half of whom may develop chronic seizures (Watson[10] and Bailey[11]).

Chronic Epilepsy Following Cerebral Injury

This series of 28 patients with chronic epilepsy due to cerebral scars, on whom operation was undertaken and adequate follow-up obtained, is subdivided as follows: cortical scars or areas of local atrophy (microgyria) following cranial injuries, 27 cases; and postoperative epilepsy following cortical resection, 1 case.

The circumscribed lesions listed above may be classified further as examples of meningocerebral cicatrices or focal lesions of the cortex with more or less involvement of the underlying brain. Air studies, which frequently revealed pronounced distortion of the underlying ventricle, showed that the pathologic process was usually a deep one, with gliosis and atrophy extending into the white matter.

In all these cases every effort had been made to control the frequency and severity of seizures by anticonvulsant drugs and general medical treatment. Operation was advised only in patients who failed to improve and in whom there was definite evidence of focal scarring shown by the aura and clinical manifestations of the seizure, neurologic examination, electroencephalogram (in the latter part of the series) and air studies.

Results following exploratory craniotomy in 28 cases of traumatic epilepsy are summarized in Table 2. In these the trauma was traced back to birth or infancy in 9. In the 19 patients in whom it occurred in later childhood or adult life, 10 had suffered depressed or compound fractures, 7 closed head injuries (2 of whom had complicating subdural hematomas that had been previously evacuated), and 1 a focal scar, the exact cause of which could not be determined. The last is included with the cases of traumatic origin for want of a better classification. In another the cicatrix was due to a previous cortical resection in the premotor area for Parkinsonian tremor. With a single exception, follow-up studies have been carried over a period of eighteen months to nine years in all cases. The final status of these patients on whom our evaluation of the results is based is presented in Table 3.

TABLE 2. *Operative Statistics in Chronic Epilepsy of Traumatic Origin.*

INJURY	NO. OF CASES	PATHOLOGIC LESION	OPERATION	EXCELLENT RESULT	GOOD RESULT	IMPROVEMENT	FAILURE
				NO. OF CASES	NO. OF CASES	NO. OF CASES	NO. OF CASES
Depressed or compound fracture ..	10	Meningocortical scar	Excision	3		1	
			Lysis of adhesions				1
		Cortical cicatrix	Excision	1	1		
			Partial excision		1		1
		Porencephalic cyst	Excision			1	
Closed head injury	7	Meningocortical scar	Lysis of adhesions	1*	2		
		Cortical cicatrix	Excision	1			
		Diffuse cortical atrophy	Lysis of adhesions	1			1
			Exploration only			1	
Previous surgery	1	Cortical cicatrix	Partial excision				1
Focal atrophy of undetermined origin	1		Excision			1	
Birth injury	9	Meningocortical scar	Excision		1		
		Cortical cicatrix	Partial excision			1	
		Porencephalic cyst	Excision	1			
			Partial excision		1		2
		Diffuse cortical atrophy	Exploration only				2
		No visible lesion	Negative exploration				1†
Totals	28			8	6	5	9

*Adhesions in this case were the residua of a previously drained subdural hematoma — small quantities of yellow fluid trapped in the subdural space, with additional lakes in the subarachnoid.

†Re-exploration has recently been carried out with localization of an epileptogenic focus by the electrocorticogram. Excision has been followed by early improvement. Again, no definite cortical scar was seen.

Post-traumatic epilepsy. Exploratory craniotomy was performed in 37 patients after old or recent injury to the brain. Of these, 28 have been under observation for prolonged periods and are suitable for this study. It is important to remember that the source of the epileptic discharge is never within the cicatrix itself, but at some point in the transition zone between the completely scarred area and normal brain. Although the cortex at this point may not appear grossly abnormal, the nerve cells are distorted and compressed by a fine network of fibroglial tissue.[2] It is impossible to locate the epileptogenic focus in the periphery of one of these scars by inspection, and the best method available, prior to the recent development of electrocorticography, was locating the area from which seizures could be induced by the thyratron stimulator with minimal current. In the smaller scars situated in relatively silent areas, the entire area was excised with a small amount of surrounding cortex.

Of 11 patients with foci that were small or so favorably situated that the entire visible cortical cicatrix or meningocortical scar could be excised, 6 have never had another seizure, and 2 others have had such a reduction in frequency and severity of attacks that they are able to work and to lead normal lives. The remaining 3 have shown definite, maintained improvement in the severity and frequency of the seizures, so that with the aid of medication all have been able to lead active lives.

In 7 patients with partial excision of the cerebral lesion, 4 failed to obtain any notable improvement. In the remaining 3, however, the results were very definitely encouraging. The following case report is of interest because the site and extent of the scar presented a particularly difficult problem:

A 21-year-old man had had a previous débridement of a gunshot wound of the left temple at this hospital in 1933. Epilepsy began 7 years later, characterized by an elaborate

visual aura (a small black bird hovering in the right upper visual field) and major Jacksonian convulsions lateralized to the right. X-ray films showed the .22 caliber bullet at the tip of the temporal lobe with the ventricle dilated and drawn toward the scar. The patient had a very slight aphasia and reduction of the right visual field. At the time of exploration (September 5, 1940) the track of the bullet was disclosed wiping out the sylvian fissure (Fig. 2). Stimulation at marker No. 4 set off a mild facial seizure with twitching of the corner of the mouth, followed for about 5 minutes by partial aphasia. We were therefore forced to content ourselves with resecting the posterior portion of the scar, where the bullet had entered, and a deeper area at the tip of the left temporal lobe. The bullet, embedded in bone, was not removed. With the exception of four major seizures, the last in 1943 after the patient had omitted dilantin, he has had only rare minor spells. In these he has to stop work in a shoe factory for a few minutes on account of a sense

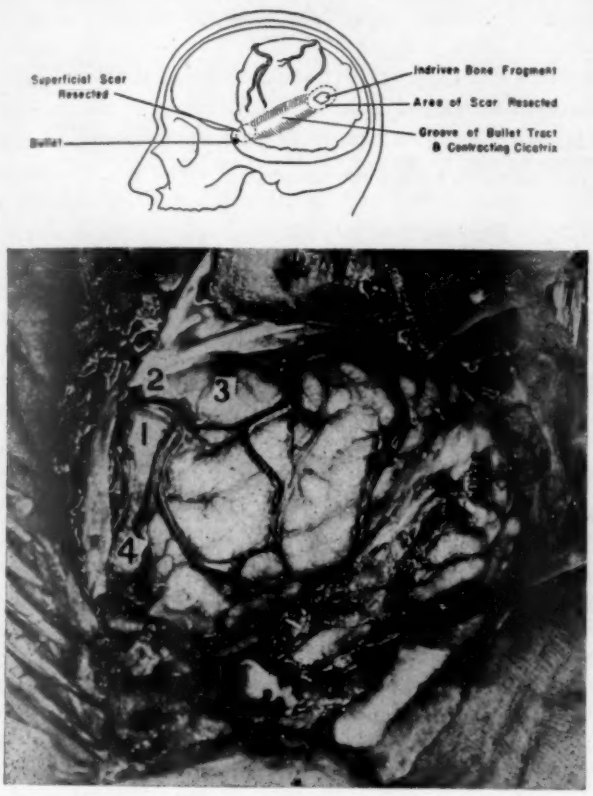

FIGURE 2. *Cortical Cicatrix in Dominant Temporal Lobe, Which Caused Major Jacksonian Seizures Starting with a Visual Aura.*

Electrical stimulation at the markers caused flexion of the fingers of the right hand (No. 1), contraction of forearm flexors (No. 2), sensation at the right knee (No. 3) and a brief convulsion limited to the face starting with movements of the corner of the mouth on the right side (No. 4).

of confusion, but can talk with difficulty. At the time of his last visit, 4¼ years after operation, he had had no seizures for 6 months.

In this decade, although accurate mapping of the motor strip could be carried out under local anesthesia with the thyratron stimulator, the method of delimiting epileptogenic areas by inducing clinical seizures through electrical stimulation was at best a crude one. At present, with the more refined methods of obtaining electrocorticograms by means of the sterile electrode holders and by mapping the spread of the after-discharge following electrical induction of a subclinical seizure (Walker et al.[4, 5]), it is possible to excise small active foci of irritable

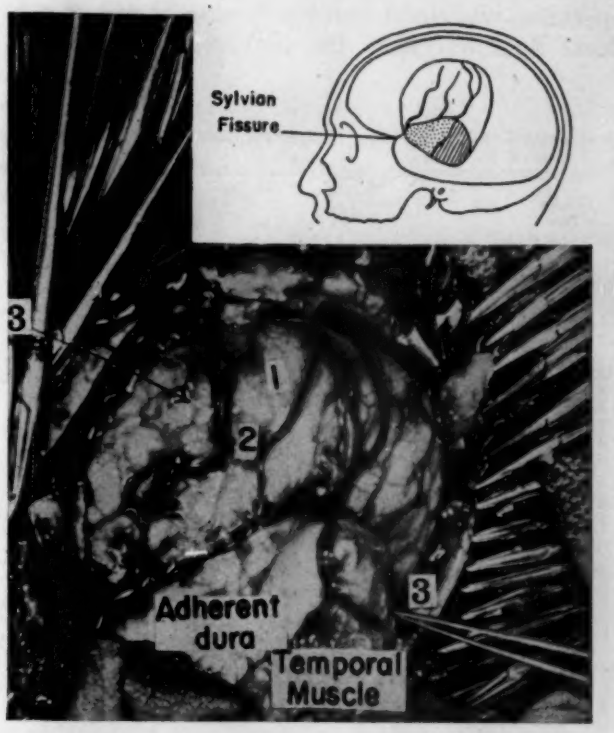

FIGURE 3. *Adherent Meningocortical Cicatrix in Dominant Temporal Lobe, Which Gave Rise to Jacksonian Seizures Starting with an Auditory Aura, Difficulty in Speech, Paresthesias in Arm and Leg and Final Loss of Consciousness.*

Electrical stimulation at Marker No. 1 caused supination and flexion of the right wrist.

Electrical stimulation at Marker No. 2 caused a low prolonged cry, followed by flexion of arm muscles and then a generalized convulsion.

Areas of abnormal-appearing cortex and pia arachnoid (Marker No. 3).

cortex at the edge of large scars even in the most important areas of the brain. Considering the difficulties of accurate localization of epileptogenic foci during this period, the complete eradication or pronounced amelioration of seizures in 14 out of 28 patients has been most encouraging.

Mere freeing up of adhesions in a meningocortical cicatrix, which was all that could be undertaken when the epileptogenic focus lay in vital speech or motor areas, was at best an unsatisfactory procedure. At present exploration can be carried farther by analysis of the cortical electrogram, whereby small epileptogenic foci can often be localized at the edge of the scar by their emission of abnormal electrical waves and excised without serious loss of function. In addition, dural repair with fibrin film

and reconstruction of cranial defects with acrylic resin plates* can now be used to reduce the reformation of meningeal adhesions that distort the vasoglial framework of the adjacent cortex. Penfield and Erickson[3] have stated that mere lysis of adhesions cannot be expected to give any significant improvement, and with this we are in general agreement. However, it is remarkable that a patient whose operation was limited to the release of yellow subdural fluid left from the previous drainage of a hematoma, with evacuation of further lakes under the arachnoid, has had complete freedom from seizures over a period of nine years. During the war he became head of the War Production Board in a large industrial city. Two other patients have been operated upon with the finding of trapped lakes of yellow fluid in the subdural space and accompanying atrophy of the underlying cortex following old closed head injury (Tables 2 and 3). After release of the high-protein-containing fluid and lysis of adhesions the former had no seizures and was working hard over a four-year period, whereas the latter has been unimproved. The difficulties encountered in the remaining case, in which dense adhesions bound the dura down to the cortex in Broca's area, are illustrated by the following report:

A 28-year-old man, after a compound depressed fracture in the left temple, developed epilepsy within 1 month. He had Jacksonian seizures for 3 years, beginning with an auditory aura, difficulty in speech and numbness and tingling of the right arm and leg, followed by loss of consciousness and biting of the tongue. At the time he left the New Haven Hospital, where the cerebral laceration was débrided and a hematoma evacuated by Dr. William J. German, he had difficulty in reading, writing and speaking, but this had improved so that on his second hospital admission here he had difficulty only when excited or at the onset of an attack. Neurologic examination was not remarkable except for slight residual aphasia. An electroencephalogram demonstrated slow waves in the left motor area, and a pneumoencephalogram showed the ventricle on the left to be slightly dilated and drawn to this side. The situation found at operation on October 19, 1948, is shown in Figure 3. The dense adhesions between the dura and cortex were divided and some areas of yellow, softened cortex in the temporal

TABLE 3. *Postoperative Follow-up Data on 28 Patients with Chronic Traumatic Epilepsy Selected for Statistical Analysis.*

Case No.	Sex	Age	Postoperative Course	Anticonvulsant Medication	Follow-up Period
		yr.			
Excision of scar with depressed or compound fracture:					
18	M	24	No attacks except immediately after operation.	No	12 yr.
28	M	12	Patient symptom free and leading normal life	No	2½ yr.
21	M	25	Patient working sporadically; no seizures, but some character change reported.	?	2½ yr.
15	M	31	Patient working	No	7½ mo.
12	F	9	Patient attending school; seizures only when medication is omitted.	Yes	3 yr.
16	F	31	Patient engaged in housework; 2 or 3 seizures yearly, but none for last 6 mo.	Yes	3½ yr.
1	M	26	Patient working hard, but has had seizures at rare intervals and one period requiring hospital admission	Yes	2 yr.
Partial excision of scar with depressed or compound fracture:					
26	M	21	No seizures on dilantin for past 6 mo.	Yes	4 yr.
13	M	15	No change; patient in corrective institution.	Yes	4½ yr.
Lysis of adhesions with depressed or compound fracture:					
22	M	28	No change in frequency or severity of seizures	Yes	8½ yr.
Excision of scar with closed head injury:					
20	M	33	No seizures, patient works as athletic coach	?	4 yr.
Lysis of adhesions with closed head injury:					
4	M	20	No seizures; patient engaged in heavy construction work.	?	4 yr.
14	M	14	Headache and 2 seizures; patient in school and is ardent athlete.	?	2 yr.
17	M	19	Patient working and looks well, but had one bout of status epilepticus (his statements may not be reliable)	No	11 yr.
24	M	26	No change in epileptic status	Yes	6½ yr.
27	M	40	No seizures; patient director of a War Production Board during war.	?	10½ yr.
Exploration only for scar with closed head injury:					
6	M	18	Definite reduction in frequency of seizures; patient able to work as farmer but has series of seizures occasionally.	Yes	6 yr.
Partial excision of scar due to previous surgery:					
3	M	25	No change in seizure pattern; recent re-exploration.	Yes	6 yr.
Excision of scar of undetermined cause:					
25	M	38	Patient does regular office work; seizures reduced to less than half their former frequency.	Yes	2 yr.
Excision after birth injury:					
23	M	15	Patient works for General Electric Company; two spells in last 6 mo.	Yes	6½ yr.
5	M	12	Patient goes to school and leads normal life; no seizures.	No	5¾ yr.
Partial excision after birth injury:					
10	M	11	About 2 seizures per month, but less frequent and severe than preoperatively; patient keeps up at school.	Yes	1½ yr.
19	M	19	Only 1 seizure per year; patient engaged in active work.	Yes	7½ yr.
9	M	3	Patient in state school and has series of convulsions about once a year; hemiplegia has increased.	Yes	9 yr.
11	F	20	Seizures continue, with progressive mental deterioration	Yes	7 yr.
Diffuse atrophy due to birth injury, no focus excised:					
8	M	8	No change in seizures	Yes	2 mo.
2	M	19	No change in seizures	Yes	9 yr
Negative exploration after birth injury:					
7	M	25	No change in seizures; second exploration recently has localized resectable focus.	Yes	8 yr.

*Cranioplasty with plates of acrylic resin is preferable to the standard method with tantalum in epileptic patients, since this material permits subsequent pneumograms to be made if continued seizures necessitate further investigation.

lobe sucked away, but at that time it was impossible to proceed farther for fear of producing a profound aphasia. There has been no change in the number or severity of the seizures.

Technical advances developed during the war have made surgical cure of cases of this sort possible. This patient will soon be readmitted, and it is planned again to free up the meningocerebral adhesions. With the cortical electrodes and direct recording of the brain waves it may then be possible to locate and excise a small epileptogenic focus at the periphery of the extensive scar without interfering with the speech areas of the dominant temporal lobe. The dura will be repaired with fibrin film to prevent reformation of a contracting meningocerebral scar, and the defect in the skull closed with an x-ray-transparent plate of acrylic resin.

Of 5 patients submitted to exploratory craniotomy, in whom diffuse areas of cortical atrophy were exposed without any clear-cut local lesion that could be excised, only 1 (Table 3, Case 6) maintained a lasting improvement of minor degree. He is able to work as a farmer, but has occasional recurrences of seizures. In several other cases, however, there was temporary improvement that might have been considered significant if follow-up observations had not been carried over prolonged periods. Brief postoperative observation in the past has often given rise to misleading conclusions, since any nonspecific operation, such as sympathectomy or even resection of the colon, has led to a temporary reduction of seizures.

When the presence of an irritable focus is well established by characteristic Jacksonian seizures and persistent abnormality in the electroencephalogram, the failure to find an epileptogenic lesion should lead to a most careful search for an underlying neoplasm. We have failed to locate such tumors in 3 cases. Pneumoencephalograms in these patients did not suggest an expanding lesion, and 2 of them gave a definite history of previous cranial injury. After the bone flap had been turned down, no very convincing cortical lesion, but only a mild degree of diffuse cortical atrophy, was disclosed in 2 cases. In the third a pinkish area with increased vascularity was observed and excised, since it gave rise to seizures on electrical stimulation. Microscopical examination, however, failed to show either gliosis or tumor. All 3 patients were regarded by the operating surgeon as tumor suspects, and careful exploration was made by palpation and diagnostic puncture. No patient had lasting relief of seizures, and all failed to return for further observation. Subsequent investigation disclosed that the first died three years later after a period of aphasia followed by coma. The other 2 were reoperated upon at other neurosurgical centers, with the discovery of an oligodendroglioma and a fibrillary astrocytoma, respectively. We have had a number of similar experiences with epileptic patients who had had a previous exploration at other clinics. Since epilepsy is frequently the first symptom of an underlying glioma or meningioma, since the seizures may persist for years without causing any rise in intracranial pressure or neurologic signs and since the pneumogram may at first be perfectly normal,[1] it is most important to bear in mind the possibility of a subcortical tumor even in a patient whose seizures have followed a definite cranial injury.

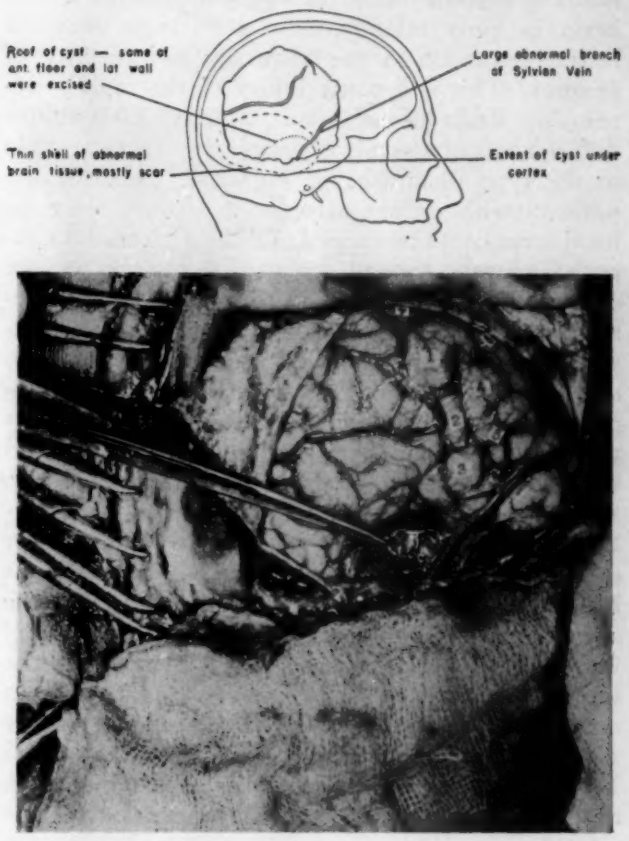
Roof of cyst — some of ant. floor and lat. wall were excised
Large abnormal branch of Sylvian Vein
Thin shell of abnormal brain tissue, mostly scar
Extent of cyst under cortex

FIGURE 4. *Large Porencephalic Cyst in a Young Woman with a Ten-Year History of Epilepsy Accompanied by a Mild Left Hemiparesis and a Homonymous Field Defect. (Seizures Began with a Sensory Aura, Followed by Turning of the Eyes and Head to the Left and Contraction of the Left Facial Muscles.)*

Marker No. 6 is on the motor strip. Electrical stimulation at the other markers induced no seizure or other response.

The statistics presented above give a good idea of the relative value of complete versus inadequate eradication of epileptogenic foci. After apparently complete excision good results were obtained in over half the patients, whereas failure to locate a circumscribed lesion in cases of diffuse atrophy was invariably followed by a continuation of the convulsive seizures. It is also of interest to break down the statistics in another way to show the results of surgery in seizures resulting from the more fre-

quent pathologic lesions that follow cerebral injury. These are presented in Table 2. From our experience with these cases we have come to the conclusion that surgical intervention can be undertaken with approximately equal chances of success in the various types of epileptogenic scars that follow trauma in the adult brain. In 11 of the 19 patients followed over adequate periods the results of surgical intervention were distinctly worth while. On the other hand, in the 9 cases in which epilepsy followed a history of birth injury or damage to the brain in early infancy, only 4 patients obtained lasting reduction in the frequency and severity of seizures. This is because injury to the rapidly developing brain of an infant is likely to produce diffuse areas of atrophy or large porencephalic cysts of the type illustrated in Figure 4. None of the patients with diffuse atrophy improved, since no focal areas could be excised. Of the 4 cases of porencephalic cysts treated by partial excision of the cyst wall and glial scar at the periphery, the results in 2 are not encouraging. Case 5, a twelve-year-old boy whose spells began at the age of three and averaged a major seizure daily, has had complete freedom for a period of five and three-quarters years. Neurologic examination is negative, and the electroencephalogram has returned to an almost normal pattern. He requires no medication and has been able to catch up with his proper grade in school. The other (Case 19), whose seizures began at the age of twelve, was operated on at the age of nineteen, and a large cystic lesion was found in the postcentral cortex. This led down to the lateral ventricle, and much of its anterior margin could not be excised owing to the proximity of the motor arm area. During the ensuing eight years he has been able to work steadily as a welder, with only occasional seizures, which disappear altogether when he remains on a careful regime with adequate anticonvulsant medication. The other patients received no benefit, and the one whose lesion is shown in Figure 4 has deteriorated mentally to the point where she should soon be committed to an institution. When birth injury results in a small cortical scar or focal atrophy (microgyria) the results of excision can be just as good as those in the adult group. Judging from Penfield and Erickson's[3] much larger series, it seems fair to conclude that in our few cases there was an unduly small proportion of eradicable lesions. Even in this least promising group the results following resection of a local scar or atrophied convolution should be distinctly worth while, provided there is not coexistent extensive atrophy of the brain.

Epilepsy after cortical excision. Epilepsy as a result of cortical excision has rarely been reported. That it may follow operations for brain tumor is a possibility, for seizures sometimes occur for the first time after the apparent total resection of meningiomas and certain circumscribed gliomas.[1] Under these circumstances, however, the epileptic disturbance has been ascribed to the tumor rather than to the operative scar. Be that as it may, this unfortunate complication does follow cases of cortical resection undertaken for the control of abnormal movements and uncontrollable tremor as seen in Parkinsonism and athetosis. Here, even with the most perfect surgical technic, a cicatrix is produced close to the motor strip, in an area that is known to produce the greatest risk of seizures. In view of the frequent enthusiastic publications of Klemme[12] the risk of such a complication is important to bear in mind. Postoperative epilepsy, which is also a complication of prefrontal leukotomy, has been reported by Freeman and Watts[13] in 4 per cent of their cases. We have encountered 2 cases in which epilepsy developed after cortical resection for tremor and have heard reports of others. In our personal cases there was a history suggestive of minor seizures before operation, the preoperative electroencephalogram was slightly abnormal, and seizures were induced in the course of mapping out the motor area prior to the cortical resection. An experience of this sort should certainly warn the surgeon against resecting the premotor area. In one of these unfortunate cases (Case 3, Table 3) we have twice reoperated and removed the more excitable portion of the scar. There was little improvement after the first operation, but after the second, in which the cortical electrode holder was used, the early results are promising.

Epilepsy after Cerebral Infection

An expanding cerebral abscess may produce acute epilepsy through cortical compression and added irritation from the zone of thrombosis and encephalitis at its frontier. In a series of 72 cases of supratentorial pyogenic abscess secondary to inflammation in the sinuses, mastoids or lungs, 9 were accompanied by acute convulsive seizures. These had a most serious prognostic import, since only 2 patients survived and these continued to have spells after healing.

In addition to the early seizures seen in the acute inflammatory stage of brain abscess discussed above, the condition has developed chronically in 11 patients with healed lesions, not all of whom were treated initially in this hospital. In only 4 of these was surgical intervention indicated and undertaken. In 1 the parasagittal postcentral scar from which an abscess had been radically enucleated resulted in seizures because of local atrophy and the formation of a porencephalic cyst communicating with the lateral ventricle. Excision of the cyst has given a good seven-year result, marred only by three convulsions at the time of childbirth. Two of the other patients operated upon had large scars binding the frontal lobe to the posterior wall of the diseased sinus. In both the scars were excised with

a narrow margin of normal-appearing brain. One, during a period of nine years, has averaged about one seizure a year, with none in the last three years. The other, whose extensive cicatrix is illustrated in Figure 5, has had no seizures in five years and has been able to work full time as a medical secretary. In a fourth case, in which an epidural abscess developed after a fracture that involved the frontal sinus, radical excision of the underlying cicatrix in the frontal lobe has given a fairly good result. Four and a half years afterward this patient was married and leading a normal life. Although she had rare seizures when off medication, these were controlled effectively by dilantin.

Summary and Conclusions

Of this series of 80 patients explored for acute or chronic epilepsy following cerebral trauma and infection, 18 have been eliminated from analysis because of inadequate periods of observation or other reasons. Of the remaining 62 in whom prolonged follow-up observations are available, definite lesions were visualized at operation in all but 1. In the acute variety the seizures were associated with intracranial clots in 15, depressed fractures in 6 and abscesses in 9. The results after cortical decompression in the hematomas and depressed fractures were uniformly good, except in cases in which there was a superimposed contusion of the underlying brain. When convulsions accompany a subdural or subcortical abscess the prognosis is extremely poor, both for the life of the patient and for relief of the seizures.

Late chronic epilepsy is caused by fibroglial scars producing meningocerebral adhesions or cicatrices of the cortex and underlying white matter. When these lesions are small and situated in relatively silent areas of the brain, the results of excision are good. If the cicatrix is a large one, or situated in vital speech and motor areas, total extirpation is out of the question. In such cases it may be possible to find a small focus responsible for the epileptic discharge. This never comes from the scar itself, but from partially damaged cortex at its periphery. In the decade from 1935 to 1944, when the surgeon had to depend on localizing the epileptogenic focus by the crude method of inducing gross seizures by electrical stimulation of the exposed cortex, our follow-up statistics show that in a series of 28 patients explored for chronic epilepsy of traumatic origin, 24 have had focal lesions suitable for surgical attack. Of these, 8 have had complete freedom from seizures for periods up to nine years. Another 6 have had a great reduction in both the frequency and the severity of their attacks, some with only an occasional seizure in the early months followed by long periods of complete freedom. All these patients are able to lead active and relatively normal lives, although they have been urged to continue taking anticonvulsant drugs. Five others have had sufficient improvement to be able to lead useful lives, whereas the remainder, including those in whom no operable lesion was found, received little or no benefit.

Three patients in whom cortical atrophy was at first held responsible for seizures later developed characteristic signs of brain tumor. Two of these had a definite history of previous cranial injury.

Postoperative results of excision of cortical scars after healing of intracranial abscesses were all that could be wished for in 1 case and very satisfactory in the other 3.

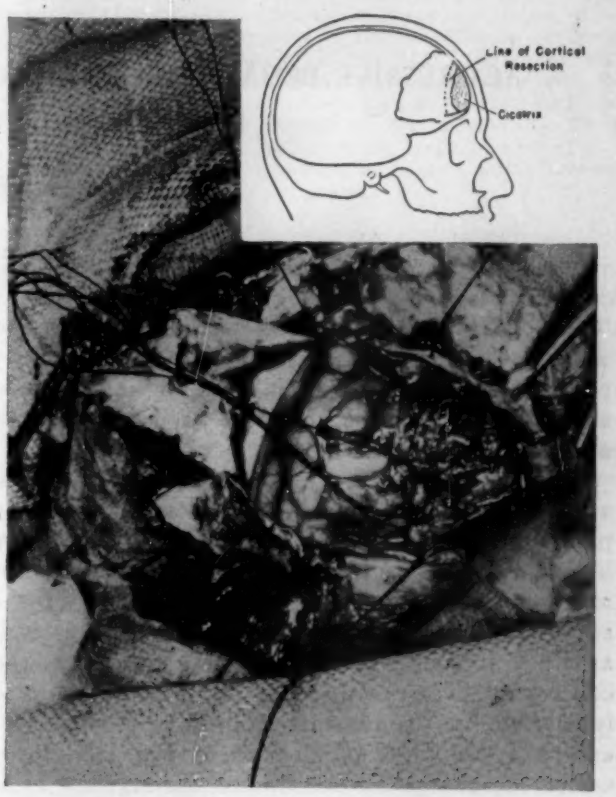

Figure 5. *Cortical Scar at Tip of Right Frontal Lobe, Resulting from Frontal Sinusitis and Osteomyelitis, Complicated by Brain Abscess Three Years Previously.*

Jacksonian epilepsy, characterized by turning of head and eyes to the left, with clonic movements of the left side, followed by generalized seizures, had been present for a year.

Recently developed means of delimiting the circumscribed epileptogenic focus with much greater accuracy by the use of direct cortical brain waves at operation and the production and mapping of subclinical seizures promise far better results. This method offers special hope in the extensive scars that are too large for total resection and in those situated in the vital speech and motor areas of the brain. As results obtained by this new technic cannot be evaluated for a period of years, it has

seemed worth while to present this statistical review of end results achieved in the preliminary period of the surgical attack on epilepsy.

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AGGRESSIVE BEHAVIOR — ITS PSYCHIATRIC AND PHYSIOLOGIC ASPECTS, ESPECIALLY IN COMBAT VETERANS*

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IMPULSIVE aggressive behavior is more frequent among the cases encountered in military psychiatric practice, especially in or near combat zones, than in civilian practice exclusive of cases appearing in combat veterans.

While serving with an overseas general hospital as chief of the neuropsychiatric section, I was impressed with the number of cases in which aggressive behavior presented the predominant symptoms and cause for admission or consultation. In the study of these cases from the psychiatric as well as from the neurophysiologic point of view, the courtesy and co-operation of Dr. Denis Hill made it possible for the patients to be taken for electroencephalographic examination to the laboratory under his charge at the Sutton Emergency Hospital. In going over the list of these patients and the causes for their admission, I find the following comments:

> "Irresistible urge to drive and wreck jeeps while intoxicated. . . ." "Brutal attack on a woman while intoxicated — had cerebral concussion when enemy shell exploded five feet from him. . . ." "Aggressive behavior while intoxicated with beer, covered by retrograde amnesia — knifed a fellow soldier who was his best friend in his organization. . . ." "Impulsive aggressiveness under alcohol; pathologic intoxication, with amnesia for entire episode. . . ." (The case of this officer, a grounded flier, will be reviewed in detail later.) "Assault and attack on a colonel while intoxicated; one previous episode of assault against a woman while intoxicated, for which he had been punished. . . ." (The differential diagnostic question was epileptic equivalent or alcoholic cerebral degeneration.) "Attempt to rape 12 women, 8 of them in one afternoon within one hour. . . ." "Insults and threats against his hutmates on the part of a staff sergeant who had consumed a not inordinately large amount of alcohol . . . ." (This patient was disarmed and put to bed and had no recollection of the episode on the following day.)

It was remarkable that with the exception of the last patient, in whom six-per-second low-voltage potentials were found in transverse leads over the parietal areas, such as were found in aggressive personalities of this type by Hill and Watterson,[1] all the patients showed completely normal cerebral electroactivity, a fact that contrasts somewhat with civilian experience. Civilian patients with brutal, impulsive, aggressive outbursts frequently show the type of "psychopathic" abnormality mentioned above, with instability of the cerebral electroactivity to physicochemical stress. It is rather surprising to find that persons with similar outbursts in military life, especially in combat personnel, tended to show these abnormalities only rarely — in only 1 case among my wartime patients. The explanation of this is probably that such outbursts of behavior are, of course, the combined results of biologic abnormality and emotional stress. If the stress is slight, the biologic abnormality has to be great to cause the abnormal behavior.

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When the stress is great, little or no biologic abnormality is necessary to produce the same result.

Another important fact was that, without exception, alcohol played a part in bringing out the abnormal behavior. In a few cases, especially in combat personnel under stress, remarkably slight amounts of alcohol sufficed to bring out the aggressive behavior reaction, but ingestion of alcohol precipitated the outburst in all. An exception was a recent case, in which the disturbance of cortical inhibitory centers, essential for bringing out this behavior pattern and usually produced by alcohol, was accomplished by another physiologic interference with cortical activity. This case is discussed below.

The types of aggressive behavior that presented themselves could be divided into the following groups:

Aggressive behavior that is directed against a specific person who incurs the patient's hostility, which is displaced, however, against another, either a similar person or a symbol of that person. An example of this type is that of a sergeant in the Air Force who received a letter from his wife telling him that since his absence overseas she had become interested in another man. He brooded over this for some time and finally wrote to his wife that he would be willing to give her a divorce. On his next day off he went to a pub with friends. After drinking not more than his usual amount of liquor, he went out into the street, walked up to a civilian couple, kicked the man and started choking the girl. Later, he had no recollection of this episode at all. His electroencephalograms were normal. He spoke of the marked resentment he felt against his wife, and it was quite obvious that in that setting he committed an act symbolic of what he wanted to do to his wife. He had had a fine military record before this incident; the only predisposing factor in his background was that his father was an alcoholic who had finally lost his home and his financial and social standing because of his drinking.

Aggressive behavior in terms of projection occurred particularly in combat personnel who had had some anxiety regarding combat and who had been temporarily or permanently released from combat duty. A rather common example of this was the flier grounded after a number of combat missions because of his increasing emotional tension. Such a man, after drinking for a while at the club, sometimes accosted another man grounded for similar reasons, abusing him verbally, pulled his gun and tried to shoot him. Here, his aggression, generated against himself, was projected and directed against another person in a similar position — especially in a setting that included drinking.

During aggressive behavior resulting when a large amount of aggressive hostility is directed indiscriminately against any and all people, the patient's consciousness is usually clouded. He is often described as having been rather subdued and not in as good spirits as usual prior to the outburst. An example is afforded by the following case:

A flier (second lieutenant), who had been under considerable combat-flying stress, was grounded because of tension and became self-critical, self-reproachful and anxious. In this state, he went to a neighboring town one evening and bought a quart of whisky to share with friends at a private club. He did not drink more than usual; he was a man who could usually handle his liquor well. He had in a somewhat subdued and tense mood consumed his usual amount of alcohol when he suddenly rose, called bystanders "Yellow, dirty Germans" and then literally tore the club apart. He was in a state of wild excitation. It took several men to restrain him, and even then he tore the buttons off the uniform of a flight surgeon who had been called to the scene. The next day he was quite subdued, tense and anxious — not on account of the incident, but just in general.

The British police have a very thorough way of taking down statements practically verbatim, as they did in this case. When I read the record of the exclamations and statements that this officer had made during the fracas, I found them to be strikingly similar to the expressions that another officer had poured forth under therapeutic abreaction by sodium pentothal; the latter officer was likewise a combat aviator, who had had two crash landings as well as other combat stress and who had become very tense. During an abreaction treatment with sodium pentothal he had suddenly given vent to a violent, aggressive emotional reaction, using almost exactly the same violent expressions as the lieutenant had used on the dance floor of the club. A comparison of the practically identical stenographic statements led to the conclusion that this lieutenant had inadvertently abreacted himself with the alcohol, which had acted on the cortex, or the outer cortical layers, in such a manner as to allow the tension and reactive aggression that had accumulated in the lower cerebral mechanisms to express themselves. The military court accepted my interpretation of the incident.

Regardless of what causes the cortical dysfunction — alcohol, sodium pentothal or any other cortical sedative or disorganizing agent — the accumulated excessive emotional pressures in the deeper centers of the brain frequently express themselves in that aggressive manner. Aggression is the natural consequence of anxiety. And in men who go through their daily combat routine, with its inevitable anxieties, there is an accumulation of aggressiveness that is bound to explode under conditions of depression of the higher cortical functions. The higher levels of the cortex, the inhibit-

ing organ, restrain the lower cortical spheres and the basal ganglions, which are the main outlets for aggression on a primitive physiologic level and probably also on a higher psychologic plane. Anything that disturbs the higher discriminating functions of the cortex will cause a release in the more primitive mechanisms, including those of the subcortex; this release in no way depends on what incapacitates the cortex. In epilepsy, for example, a great deal of abnormal cortical electroactivity is present, which may indicate a degree of cortical disturbance sufficient to interfere permanently or temporarily with the higher discriminating functions of the cortex. In patients with focal brain lesions there is usually only focal abnormal cortical electroactivity. The ingestion of alcohol may cause the abnormality to spread from its focal point to envelop the entire cortex, normally a source of controlling influence, and the entire cortex may become temporarily worthless. In the presence of emotional disturbance, especially anxiety and tension, the disorganization of cortical discriminating functions by alcohol alone is sometimes sufficient to release aggressive outbursts. In both of the two latter instances, one speaks of "pathologic intoxication." In "normal intoxication," there is a proportionate inhibition of cortical discriminating functions and of activity, including aggressive activity.[2]

I have encountered interesting cases of eruption of aggression in veterans after their return to civilian life. One of the surprising features in these cases is the understanding sympathy and tolerance of the patient's relatives. An example is provided by the following case of a husband who cut his wife's throat with a razor, for which act he is now serving a sentence at the state prison colony. His wife holds no grudge against him but considers the assault a symptom of his emotional illness — certainly a most enlightened view on the part of the victim. This view was not shared by the court.

The patient had been an ammunition loader in the Pacific Theater and had performed his duties well until the time when he was unloading an ammunition ship in the Aleutian Islands and had to get off the ship in a hurry because of an approaching storm. He slipped and fell 25 feet to a barge below. He was unconscious for 10 minutes, bled from the nose and injured his left hand. Shortly after this episode he developed nervous excitability and headaches, which soon became disabling; he was sent home and discharged for neurosis.

One evening when he dined out with his wife he consumed three mugs of beer and a "shot" of whisky. His manner was calm, and they had no arguments. On returning home his wife lay down for a nap, and he covered her with a blanket. About ½ hour later she was suddenly awakened by a sharp pain. Blood was flowing from a long, deep cut on the right side of her neck (a 4-inch scar remained as evidence when I saw her 8 months after the incident). Her husband was standing over her, staring at her, a razor blade in his hand. When she asked him what he had done he did not answer but went to the closet, got a clean towel and wrapped it around her neck to check the bleeding. Then he ran out and gave himself up at the police station. All the patient remembered about the incident, however, was covering his wife with a blanket when she first lay down, and the next thing he knew "she was lying there bleeding, and I ran out of the house for help." He was observed at the metropolitan state hospital and was considered legally sane but suffering from "psychoneurosis." He was tried and convicted for assault.

When I examined him at the state prison colony I found a man of small stature, extraordinarily tense, anxious and jittery, as well as definitely depressed. His sleep was still haunted by nightmares; he frequently dreamed of loading an ammunition ship, of somebody yelling, "Get off quick!" and then of awakening from the explosion, which usually turned out to be a slammed door or a similar noise. However, he was free of guilt feelings about his deed "because I did not know what I was doing at the time — I just pleaded guilty because the lawyer told me to." He did think that he had made other mistakes. He felt he should have stayed in the Army, and had a stronger guilt feeling about that than about attacking his wife.

Neurologic examination revealed normal findings — especially, normal Achilles reflexes and vibration sense. My diagnosis was: "psychoneurosis, anxiety-tension state, severe." The recent history suggested that marked unconscious, repressed aggressiveness had erupted under cortical sedation by a small amount of alcoholic beverages, producing a state of pathologic intoxication.

In the cases discussed above, cortical dysfunction was always affected by alcohol. Hill[3, 4] found that in cases in which there was a focal abnormal cortical electroactivity, ingestion of alcohol — especially beer — made this abnormal electroactivity spread all over the cortex. Hill[3, 4] has likewise shown that with ingestion of a similar amount of water, especially in cold weather, which facilitates hydration of tissues, the same result could be obtained. In a case of matricide described by Hill and Sargant[5] aggressive behavior associated with abnormal cerebral electroactivity resulted from the combined effects of low blood sugar and hyperventilation incidental to a violent argument.

I was recently asked to examine a combat veteran who had committed an unreasonable aggressive act that was not in keeping with his personality or his situational needs. He had been under tension incidental to frustrating experiences after his return to civilian life — he had not succeeded in getting into the college of his choice, he had not obtained the job he wanted, and his girl had jilted him while he was overseas. About his state of mind after his return in January, 1946, he said, "I was unsettled. I wanted so much, but nothing was panning out. It wasn't what it was cracked up to be. A lot of things I didn't want to happen did happen." This case is reported in detail, as follows:

In March, 1946, this 21-year-old man started working 9 or 10 hours daily in a cold-storage plant at −10 to −15°F. When he left the plant after work, at first he was chilly for ½ hour and then became uncomfortably warm, and if he engaged in any exercise he "perspired to beat the band while my friends would be dry as a bone." This feeling usually subsided during the night.

One evening after coming home from work, he changed to his dungarees and field jacket, stuck an unloaded German Luger pistol into his belt (for which action he had no explanation) and then drove around for several hours and vaguely headed toward the home of the girl who had jilted him, but on the outskirts of the town he turned and drove back toward Ft. Devens and then to Littleton, where he stopped at a store for a package of cigarettes.

In reaching for his wallet in his back trouser pocket, he exposed the gun in his belt, and when he noticed that the storekeeper became frightened and panicky he was surprised, for he had forgotten that the gun was there. "I did

not know exactly what to do, so right off I backed away, pulled out the gun, and said, 'Give me the folding money.'" The storekeeper gave him about $20, which he put in his wallet, where he had $47 of his own. Then he ran out and got away in his car, but a police car that was parked across the street chased and caught him. He surrendered, was very co-operative, helped the police look for the gun, which he had thrown from his car window, and in every way acted his usual polite self.

The robbery occurred at 10:00 p.m., after he had been driving around seemingly aimlessly for about 3 hours; he had left the cold-storage plant at about 5:30 p.m. He could give no motive for his crime. He had sufficient money of his own — about $1000 in accumulated pay. His family, with whom he lived and with whom he was very congenial, were of good middle-class circumstances, owned their own home and car and were capable of supplying a college education for their children. The patient himself was a clean-cut, tall, personable young man who had been outstanding in high-school athletics and who on the basis of his intelligence, ability and personality assets, as well as on his own and his family's standing in the community, was entitled to look forward to a happy and successful development. He had never committed any criminal acts before, had been a good student in high school and had shown no signs of psychopathic instability in the past. There was no record of truancy or disorderliness. His war record was excellent; he had been a sergeant in the combat engineers attached to the Fourth

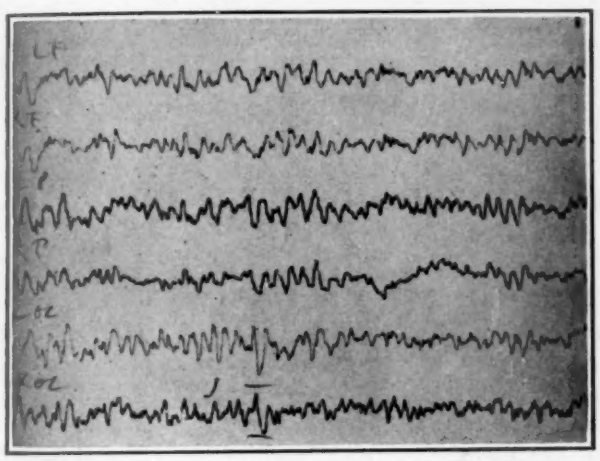

FIGURE 1. *Electroencephalogram Taken before Exposure to Cold.*

The six leads are shown in the following order: left frontal, right frontal, left parietal, right parietal, left occipital and right occipital.

Armored Division, holding the rating of platoon sergeant from August, 1944, to January, 1946.

The history of his combat experience disclosed an incident of concussion with unconsciousness followed by a state of probable postconcussional confusion lasting 3 hours on February 4, 1945. This occurred during the battle of the crossing of the Saar River when an enemy shell struck a rocky ledge near his head. This instance of confusion was probably organic since it was not followed by any disturbance during subsequent combat activity (he afterwards participated in the Battle of the Rhine), as would inevitably have occurred had the incident been a neurotic fugue state.

Physical and neurologic examination revealed weakness of the right lower facial muscles, disturbance of abdominal reflexes on the right (the right upper being frequently absent, and the right middle and lower showing early exhaustibility); the right plantar reflex was abnormal, showing dorsiflexion of the great toe associated with outward rotation of the thigh and leg, and contraction of the fascia lata without fanning of the small toes.

Psychiatric examination demonstrated excellent general intelligence, and nonverbal testing by the Kohs block test revealed a mental age of 18¼ years. However, his vocabulary level was reduced to one of 15½ years. A reading test revealed the presence of a moderate amount of dyslexia. There was some deterioration of the fund of knowledge, especially of history. All this contrasted with his high-school record of A's and B's in English and history. His blood pressure was elevated to 160/90.

Emotionally, the patient presented a superficially calm appearance, with a good deal of tension and resentment coming to the fore on psychiatric exploration.

Electroencephalographic examination, which was performed at Dr. Lennox's laboratory, revealed a focus of abnormal

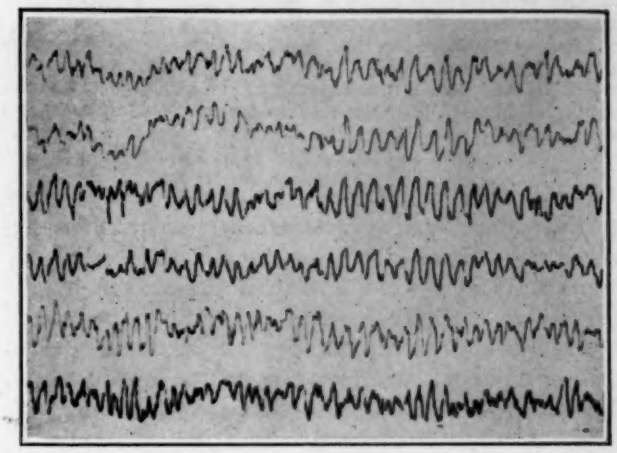

FIGURE 2. *Electroencephalogram Taken Four and a Half Hours after Exposure to Cold through Seven Hours with Alternating Periods of Twenty to Thirty Minutes Spent In and Outside a Cold-Storage Room with a Temperature between −10 and −15°F.*

The six leads are shown in the same order as in Figure 1.

cerebral electroactivity with high-voltage, slow discharges at the rate of 5 or 6 per second, some of them square-topped, and diphasic slow spike discharges involving both occipital and parietal regions, more marked on the left (Fig. 1).

The aggressive outburst had occurred along the line of least resistance — namely, after the storekeeper had shown fear. In other words, the accumulated aggression, which was directed against those responsible for his frustrations and which the patient had held within him, had erupted toward the one man who had shown any fear of him.

From a study of the total personality it was believed that some organic factor was responsible for the patient's obtaining so much cortical release — that is, so much relaxation from his usually upheld behavioral standards in life, which are a function of his cortex. He was thoroughly questioned regarding whether or not he had been taking alcohol prior to the aggressive outburst. It was explained to him that whether he had been drinking or not would not make much difference from the medicolegal point of view, and the concept of pathologic intoxication was explained to him, but he steadfastly maintained he had had no liquor that day or even that week, that although he was not a teetotaler, he drank only on rare social occasions, that he did not derive particular pleasure from alcohol, and that he had throughout his military life abstained except on occasional passes and leaves because he felt that his position as platoon sergeant necessitated such abstinence.

The patient's actions on that day and his daily routine were reviewed. I then believed that it would be worth while investigating whether his occupational exposure to cold had any effect on his abnormal cerebral electroactivity. There is evidence,[6] that the action of cold on cerebral electroactivity is similar to that of metrazol or eserine[7] and that in man shock from exposure to cold may be associated with tonic-clonic convulsions. These findings prompted Noell[7]

and others to advise against the use of analeptic stimulants such as metrazol and camphor for the treatment of shock from exposure to cold.

It was arranged for the patient to return to the cold-storage plant, to spend a day there under conditions of observation with recording of his temperature, and to follow it by another electroencephalographic examination. It was found that the patient's temperature, which was 98°F. at the start, fell to 97.2°F. after 1 hour and to 97 after 3 hours' sojourn in the cold-storage room (in spite of 30-minute interruptions as usual in his work); it remained 97°F. until he emerged at the end of the day, whereupon it began to rise gradually to 97.6°F. 1 hour after emerging, to 98°F. 2 hours after emerging, and then continued till it reached 99°F. 4 hours after he emerged, staying at that level for an additional 5th hour and then gradually falling back to normal, his normal temperature of 98°F. being reached 8 hours after emergence from the cold room.

The electroencephalogram was taken during the 5th hour after emergence — which was the approximate time at which he had committed the crime. It was found that the abnormal high-voltage activity had spread to all leads, in a way similar to what might have been expected from the effects of metrazol, eserine, alcohol or hydration (Fig. 2).

It was concluded that in this case heightened subcortical emotional aggressiveness was released because the cortical inhibitory centers had been disorganized, not by the effects of alcohol but by the effects of exposure to cold, which had permitted the abnormal electroactivity of a circumscribed traumatic focus to spread over the entire brain. No attempt was made to determine whether this spread was actually the direct consequence of the cold or the consequence of the hyperthermic response elicited by the exposure to cold.

On the basis of these facts, which were presented to the Court, the patient was given a suspended sentence with a probationary period of two years.

Conclusion

The study of aggressive behavior is a field of neuropsychiatry characterized by a remarkable degree of interplay of psychiatric and physiologic forces, the unraveling of which demands an understanding of the psychiatric as well as of the physiologic aspects of behavior.

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PRIMARY TERATOMATOUS CHORIONEPITHELIOMA OF THE OVARY*

Report of a Case

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CHORIONEPITHELIOMA of the ovary may arise from two fundamental sources: a pregnancy, uterine or ectopic; and a teratoma. It is our purpose to discuss only the latter, and to add a case to the literature.

Pick,[1] in 1904, described a nine-year-old girl whose abdomen revealed a teratoma of the ovary with mesodermal, entodermal and ectodermal components, and pure chorionepithelioma. Since then 12 other proved cases have been reported,[2–13] only 3 of which are reviewed in the American literature.[3, 12, 13] A few other cases must be eliminated because they followed pregnancies and may have represented metastases from uterine chorionepitheliomas that regressed spontaneously, were expelled with the placenta[14–27] or were removed by the curette.[28] A primary ovarian chorionepithelioma can be assumed with certainty only in a child.[7] Nine of the cases reported, including the one presented below, occurred in children before the age of puberty. Four of these (Table 1) presented evidence of precocious sexual development, and a fifth had uterine bleeding. In such cases a diagnosis can be made clinically since a positive pregnancy test (Aschheim-Zondek or Friedman) is diagnostic of teratomatous chorionepithelioma,[13] especially with dilute urine and spinal fluid. Other cases presented no typical symptoms, and 2 cases were diagnosed as appendicitis.[4, 6] Because of the age and the positive pregnancy test, the cases of Fasold,[5] Bettinger,[6] and Tscherne and Schäffer[9] are accepted as chorionepithelioma of teratomatous origin even though histologically no teratomatous elements were found. In adults the picture is that of ectopic pregnancy with irregular vaginal bleeding and the finding of an abdominal mass.

Treatment in such cases is unsatisfactory, and the longest recorded survival after operation is eight months.[13] Since the diagnosis is usually made postoperatively, the proper course is controversial. The consensus is that complete operation with removal of the uterus and other ovary is indicated

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if there is no x-ray or hormonal evidence of metastasis.[29–31] Crossen[32] prefers surgery to radiation, which is of little value in this type of tumor.

The following case of teratomatous chorionepithelioma of the ovary is considered worthy of report because of the rare occurrence of this type of neoplasm, with a scarcity of reports in the literature, and because of the hopeless prognosis offered, irrespective of the type of treatment administered.

TABLE 1. *Proved Cases of Primary Chorionepithelioma of the Ovary, according to Year of Publication.*

AUTHOR	YEAR	AGE OF PATIENT	SYMPTOM	SURVIVAL AFTER OPERATION
Pick[1]	1904	9	Abdominal swelling	Few weeks
Albrecht[2]	1913	18	Abdominal mass	5 months
Read[3]	1928	11	Abdominal pain	1 month
Freund[4]	1929	7	Abdominal pain	?
Fasold[5]	1931	8	Precocious sexual development and vaginal bleeding	?
Bettinger[6]	1932	7	Pain in pelvis, precocious sexual development and vaginal bleeding	?
Siegmund[7]	1932	6	Precocious sexual development and vaginal bleeding	5 weeks
Fikentscher[8]	1937	14	Vaginal bleeding	?
Tscherne and Schäffer[9]	1939	8	Vaginal bleeding and precocious sexual development	2 months
Sbarcea[10]	1939	27	Vaginal bleeding	10 weeks
Oda et al.[11]	1940	11	Abdominal mass	?
Backus and Griffin[12]	1941	13	Right-lower-quadrant pain	6 months
Sturley[13]	1942	19	Vaginal bleeding	8 months
Oliver and Horne	1947	11	Abdominal pain	4 months

CASE REPORT

S. F., an 11-year-old Italian girl, was first seen in the accident ward of the hospital on December 12, 1946, complaining of low abdominal pain. She was observed for 24 hours and discharged, improved, with a diagnosis of mesenteric adenitis. She returned to the hospital on January 19, 1947, again complaining of low abdominal pain, which had suddenly occurred 5 hours before admission and was limited to the hypogastrium. The pain was constant, dull and not accompanied by nausea, vomiting or bowel change. There were no urinary complaints, vaginal discharge or bleeding. Neither chills nor fever had been noted, and the patient had never menstruated.

Other than the usual childhood diseases, no serious illnesses had been contracted and the family and social histories were irrelevant.

Physical examination revealed a thin, but well developed girl, who was in no acute distress. The heart was within normal limits, and no murmurs were present. The lungs were resonant throughout, with no rales or abnormal breath sounds. Palpation of the abdomen revealed an ill defined, lemon-sized mass in the right lower quadrant, which extended 5 cm. above the symphysis to the right of the midline. It was freely movable, hard and nontender. No muscle spasm or fluid wave was present. The vaginal orifice was infantile, but rectal examination disclosed a rather firm mass bulging into the rectum; it did not appear to be attached to the uterus. In view of the fact that the patient had had a similar attack 6 weeks previously it was believed that she had appendicitis, with rupture and abscess formation, although the white-cell count was only 6400, with 61 per cent neutrophils, and the sedimentation rate 35 mm. in 1 hour.

The temperature was 98.6°F., the pulse 100, and the respirations 20. The blood pressure was 85/55.

On January 21 a laparotomy was performed under nitrous oxide, oxygen and ether anesthesia through a low-midline incision. The appendix was easily located and found to be normal. On further exploration, a large hemorrhagic necrotic tumor of the right ovary was clearly visualized. It proved to be densely adherent to the right posterior peritoneum, and extended deep into the pelvis. The entire mass, including the right tube, was dissected free and removed without difficulty. No gross evidence of metastasis was noted. The uterus, left tube and left ovary appeared normal.

The immediate postoperative course was uneventful. On the 3rd postoperative day the patient began to menstruate for the first time, and although bleeding was not excessive, the hemoglobin gradually fell to 49 per cent and multiple transfusions of whole blood were given. Except for continued weakness, she was apparently in good condition. Further surgery was considered to be inadvisable until a positive pathological report of a malignant lesion could be verified, and radiation therapy was considered only as a last resort. A Friedman test was negative on February 1, but strongly positive on February 10 and positive with spinal fluid on February 17. No evidence of metastases was found by x-ray examination on January 29 and February 15 and 22. X-ray therapy was started on February 26, and continued through March 25. The patient received twenty-one treatments for a total of 4000 r given in four different fields. The hemoglobin continued to remain between 50 and 60 per cent,

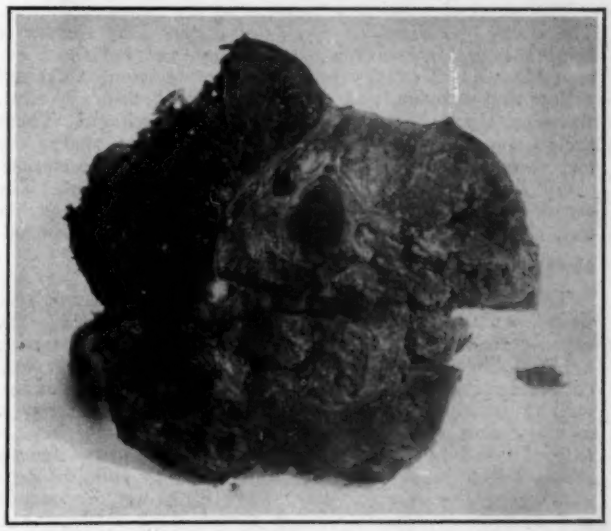

FIGURE 1. *Photograph of the Tumor of the Ovary.*

despite repeated small transfusions until March 23, when she had improved clinically to the extent that she was afebrile and asymptomatic with a rise in hemoglobin to 75 per cent. She was discharged on the 65th hospital day. The Friedman test remained strongly positive with dilutions of urine, uninfluenced by the radiation therapy. By April 15 she was losing weight and was unable to return to the tumor clinic for follow-up examination. Her family physician stated that a nontender mass had developed in the lower abdomen and gradually enlarged, reaching to the xiphoid process before death. The patient expired suddenly 4 months after operation. Permission for autopsy was not granted.

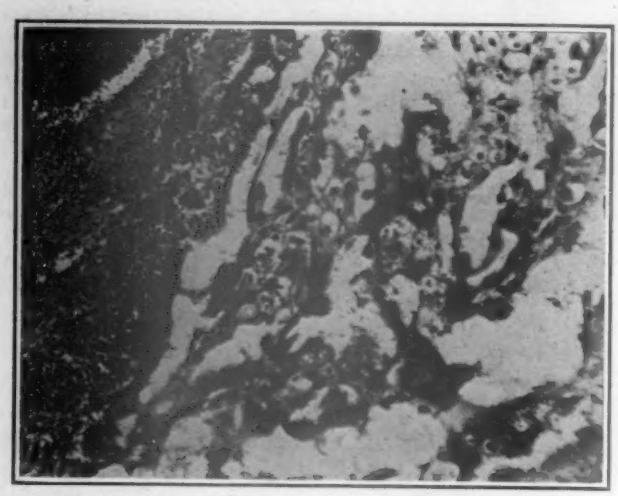

FIGURE 2. *Photomicrograph of the Ovarian Tumor, Showing the Islands of Langhans and Syncytial Cells Imbedded in Hemorrhagic Tissue.*

Macroscopic examination was as follows (Fig. 1):

The surgical specimen consists of an ovary and tube. The ovary measures 7.5 by 7 by 7 cm. The surface is smooth and shiny with a mottled blue and red sheen except for a small shaggy area. On section, some areas are yellow and caseous, and others are dark brown and firm. Between these areas the surface is hemorrhagic. There are numerous cysts scattered throughout the ovary, the largest measuring 2 cm. in diameter. They have a smooth shiny lining. The tube measures 5.5 by 0.5 cm. The serosa is smooth and glistening, the lumen patent throughout, and the mucosa normal. The mesosalpinx is normal.

Microscopical examination was as follows (Fig. 2):

The capsule consists of partially hyalinized connective tissue, which contains foci of lymphocytes. Beneath the capsule are scattered areas of normal ovarian stroma with a few follicles lined by a single layer of columnar and cuboidal epithelium. The macroscopic cysts have a definite wall of stratified squamous epithelium. The greater part of the cortex and medulla, however, is markedly hemorrhagic, with large areas of necrosis. Adjacent to the hemorrhagic areas are several masses of round to cuboidal cells varying greatly in size. They have a distinct cell outline and a clear cytoplasm with a round, dark nucleus, and represent Langhans cells. These cells are separated into small clusters by large cells, which have an indefinite cell wall. They are deeper staining and contain irregularly shaped, dark nuclei, some of the cytoplasmic masses being multinucleated. These represent syncytial cells. Mitoses are not seen.

SUMMARY

A case of primary teratomatous chorionepithelioma of the ovary in a young girl is reported. This appears to be the fourteenth authenticated case report, none having been reported in the past four years; only 3 other proved cases have been found in the American literature. The diagnosis was not made preoperatively, and the gross disease was difficult to recognize. Evidence of precocious sexual development was not noted.

The prognosis is poor as illustrated in the case reported, death occurring in all cases in less than a year. Removal of the uterus and other ovary at the time of the original operation might have prolonged this patient's life, although this point is controversial even among leading gynecologists. Treatment at its best is unsatisfactory. More case reports should be forthcoming if this interesting tumor, which presents an unfavorable outcome, is to be recognized.

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YAWS IN MASSACHUSETTS*

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YAWS can occur in Massachusetts. Several physicians refused to believe this possibility and doubted the history given on several occasions by the mother of the patients in the cases reported below. The return of overseas veterans and the rapidity of transportation increase the likelihood of sporadic cases of tropical diseases. A carefully taken history, including recent change of abode, is important. The diagnosis in both these cases was promptly made by the original observers in Jamaica.

Ease of transmission, owing to abundance of the etiologic agent on the exposed skin, makes yaws a serious disease in crowded neighborhoods. It must be considered in the differential diagnosis of persistent granulomas. History, dark-field examination and serology of a patient presenting echthymatous lesions will readily establish the diagnosis, especially in children, because it is a nonvenereal disease.

CASE REPORTS

CASE 1. E. R., an 8-year-old Negress, was seen in the Boston City Hospital Out-Patient Department on September 24, 1947, complaining of sores on the right heel and left buttock. The history revealed that her family had lived on the island of Jamaica, British West Indies, from 1945 until August, 1947. On April, 1946, she had stepped on a tack, and a crusted area had subsequently appeared. It persisted for months until the patient was seen by a district nurse, who diagnosed the lesion as yaws. The diagnosis was confirmed by laboratory studies at the hospital, and treatment consisting of a few doses of bismuth and salvarsan was given. After the first treatment, the patient suffered a generalized "measle-like" eruption, which with the initial lesion disappeared after treatment. In July a blister appeared on the right heel and became crusted. It was present on her return to the United States in August, and assumed the appearance seen on September 15. The lesion was circular, 3 cm. in diameter, elevated, crusted and indurated, with a surrounding ring of satellite vesicles (Fig. 1). Dark-field examination showed treponemas. Further examination revealed a similar lesion on the left side of the intergluteal fold (Fig. 2). The blood Hinton test was positive. The patient was given 4,000,000 units of penicillin.

FIGURE 1. *Photograph of the Right Heel in Case 1, Showing an Inverted Saucer-like Granuloma.*

Dark-field examination of the serum showed Treponema pertenue.

FIGURE 2. *Photograph of the Left Buttock in Case 1, Showing the Frambesiform Lesion of Yaws.*

CASE 2. D. R., the 5-year-old brother of the patient in Case 1, was seen on October 10, 1947, when examination showed a sore on the left heel and left buccal mucous membrane. The history revealed that 6 months previously, while living in Jamaica, he had injured his leg, and a lump that crusted had appeared. It was diagnosed as yaws, and he received three injections of bismuth and seven injections of salvarsan. The lesion had healed when he returned to the United States in August. On October 1 the left heel had broken down, and his mouth became sore. Examination showed a small superficial ulceration on the left buccal mucous membrane and an indurated, crusted ulcer, 1.5 cm. in diameter, on the left heel. Many enlarged nontender nodules were present in the post-cervical area. Dark-field examination showed many treponemas. The blood Hinton test was doubtful on October 10 and strongly positive on October 15. This patient was also given 4,000,000 units of penicillin.

DISCUSSION

In the differential diagnosis of persistent granulomatous lesions, in addition to reactions to drugs

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including bromides, syphilis, tuberculosis and deep-seated mycotic infections, yaws must be considered. Although it is endemic in the East and West Indies and equatorial areas, sporadic cases may be seen in the United States.

The primary lesion is almost invariably extragenital, occurring most often on the lower extremities, usually at the site of recent injury. *Treponema pertenue* is the etiologic agent that invades the blood stream. The primary lesion is found, after three or four weeks' incubation. It is usually an elevated ulceration with constant crusting. The secondary lesions start as macules, becoming papules and later typical frambesiform lesions. These are elevated nodules, from 1 to 2 cm. in diameter, often covered by dried serum. When this dried serum is washed off, a round, pink, lobulated surface resembling a raspberry is seen. Such a lesion was present on the patient's heel in Case 1. Washing the surface of a crusted ulceration with soap and water is often very revealing. It may show a carcinoma, syphilis, yaws or blastomycosis, all of which have characteristic clinical pictures. Penicillin apparently successfully arrests this disease and perhaps cures it.

SUMMARY

The possible occurrence of yaws in Massachusetts, as well as the points to be considered in diagnosis and treatment, is briefly discussed.

Two cases that occurred in residents of Massachusetts who had lived in Jamaica are reported.

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MEDICAL PROGRESS

MALARIA*

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IN 1943 an article was written to review the significant concepts and facts about malaria among human beings.[1] In that account, a brief allusion was made to the comprehensive program placed in operation by the armed forces to control malaria. Nothing could be said at that time about the extensive mobilization of clinicians, chemists, parasitologists and entomologists and the training of skilled personnel to attack unsolved malarial problems, which were of extreme strategic importance to the Allies.

Sufficient time has elapsed since the close of World War II to evaluate the foremost advances made in the knowledge of malaria in human patients during and since the conflict. The majority of advances arose out of laboratory and field solutions to problems of diagnosis, prophylaxis, treatment and control that confronted the armed forces fighting in tropical areas. Fortunately, many of the advances, particularly in chemotherapy, were made and applied in time to aid in tipping the balance in favor of the Allies during operations in malarious areas. In the words of Russell[2]: "Military experience taught once more that the prevention of malaria is neither automatic nor simple but is compounded of law and persuasion, organization and training, supplies and technical applications."

The necessity of war forced the expenditure of large sums of money, which speeded the production, organization and application of newer insecticides to the drastic control of malaria in heavy malarious areas. The results have been so satisfactory that malariologists are predicting the complete eradication of malaria from this[3] and other countries[4] if the new weapons for control are used wisely. A discussion of the development of insecticides and methods for their use against malarial vectors and other arthropods that transmit tropical diseases is not within the scope of this paper. It is sufficient to say that the continued intelligent and skilled uses of the newer methods of mosquito control and the proper use of new antimalarial drugs will go far in reducing the menace of malaria to that of a minor tropical disease. Unfortunately, the existence of lethal insecticides and effective antimalarial drugs does not guarantee their proper use in hyperendemic malarious areas where the problem equals that which existed prior to World War II.

The purpose of this article is not to give a comprehensive account of progress in malariology or to argue in favor of new methods for the treatment of malaria and the control of anopheline mosquitoes. The contributions considered add to the basic knowledge of the parasites, to clinical knowledge of the course and sequelae of the disease so that a prompt diagnosis can be made and to methods of treatment.

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The Parasites

Pertinent information about the mechanism of disease production by malarial parasites was reviewed previously.[1] The precise biochemical basis for the interpretations is just beginning to unfold. Growth and multiplication of mammalian plasmodia in vitro have been obtained,[5, 6] and the methods developed for the studies have provided tools to determine the physical and chemical requirements for growth and nutrition of the parasites.[7, 8] The medium developed for these studies is the result of attempts to devise a synthetic plasma, containing inorganic salts, sources of calories such as glucose, glycerol and sodium acetate, amino acids for protein synthesis, vitamins, para-aminobenzoic acid, purines and pyrimidines. Of these substances, glucose, para-aminobenzoic acid[8] and methionine[9] have been established as essential nutrients for *Plasmodium knowlesi*, and the other ingredients appear to be accessory growth-promoting compounds. These studies also showed that the malarial organism cannot survive on the available hemoglobin and cytoplasm of the red cell. The plasma must supply other nutrients for diffusion through the cell membrane if the parasite is to grow and metabolize normally and produce progeny or merozoites for reinvasion of other erythrocytes. Thus, there are plasma or host factors that control levels of parasitemia and perhaps pathogenesis of malarial parasites.[10]

In 1943 and 1947 Trager[11, 12] reported on the effect of biotin and a biotin-like substance upon susceptibility to avian malaria. This work was confirmed and extended by Seeler and his collaborators[13–16] to experiments with riboflavin, thiamin, folic acid and protein deficiencies. Rigdon[17] failed to detect any effect of vitamin A deficiency on *P. lophurae* in ducks.

The cultural studies with mammalian parasites in vitro have pointed the way to a further extension of studies in vivo. Monkeys (*Macaca mulatta*) deficient in ascorbic acid[18] will control spontaneously an infection with *P. knowlesi*. The absence of methionine from the diet of monkeys and monkeys on fast will also control this highly pathogenic organism.[19] This work is of fundamental importance and the results of more experiments will be followed with interest.

Direct biochemical studies of suspensions of avian and mammalian plasmodia show that the parasitized erythrocytes consume twenty-five to seventy-five times more glucose than the normal red cells.[20, 21] *P. knowlesi* and *P. gallinaceum* contain proteolytic enzymes, which are capable of splitting, degrading[17] and synthesizing protein.[21, 22] The finding that *P. gallinaceum* produces amino nitrogen and ammonia as by-products of protein and glucose under certain conditions[22] might lead the way to studies that will prove or disprove the production of "toxins" by malarial parasites.

The sequence of events in avian malaria between the bite of an infected mosquito and the blood stages of the parasites has been worked out in detail by Huff and Coulston.[23, 24] These studies are outstanding contributions to malariology. Infective mosquito stages of the malarial parasite, *P. gallinaceum*, were inoculated into young chicks. The chicks were killed at given time intervals and examined histologically. In this way the precise development of the sporozoites (infective stages) through stages called cryptozoites and metacryptozoites within fibroblasts and other lymphoid cells was discovered. The stages resulting from this tissue development emerged later into the blood stream to reinvade the erythrocytes. Although similar stages have not been found in any of the malarias occurring in human beings, they have been found[25, 26] in the parenchymal cells of the liver in monkey infections with *P. cynomolgi* and verified by Hawking.[27]*

It is believed that such tissue stages exist at least in benign tertian malaria (*P. vivax*) of man and that they are the basis for the serious relapsing nature of this type of malaria. The exact reasons for the relapsing nature of *P. vivax* have not been determined satisfactorily. The explanations that are accepted at present are based by inference on experiments in vivo conducted before the war and later during the war by Fairley and his collaborators[28] in Australia and by the discovery of the so-called "tissue stages" in avian malaria mentioned above. The infective stages, or sporozoites, injected by female anopheline mosquitoes, do not enter the circulating erythrocytes immediately. Patients inoculated experimentally by infected mosquitoes did not have circulating blood parasites from about thirty-six hours to times ranging from two hundred and six to two hundred and fifty-four hours after the infective bite. This was proved by transfusions of large quantities of blood (200 to 500 cc.) from infected patients to normal persons. Parasites could be found on an average of twelve days (range, ten to seventeen days) after exposure. These results indicated that tissue stages of *P. vivax* must exist and that the time required for their appearance differs with species and perhaps strains of parasites.

Similar experiments with *P. falciparum*[28] gave negative blood tests up to one hundred and forty-four to one hundred and sixty hours after the infective bite, and parasites could be demonstrated seven to twelve days after the bite.

It is also believed that the inability to obtain radical cures of relapsing tertian malaria with antimalarial drugs is due to the failure of these drugs to penetrate and exert a lethal action on tissue

*Since this paper was received for publication the tissue stages of *P. vivax* have been discovered and described by Professor Shortt at the Fourth International Congresses on Tropical Medicine and Malaria.

stages of the plasmodia. The ease by which it is possible to cure benign tertian malaria in paretics who receive their infection by the passage of infected blood gives credence to the theory. These patients receiving malaria induced by blood passage have no tissue stages, and therefore radical cures can be effected with antimalarial drugs. It remains to be determined experimentally whether or not the ability to obtain radical cures of naturally acquired malignant tertian (*P. falciparum*) infections with drugs (a point discussed below) means that the hypothetical tissue stages do not exist or that they are more susceptible to drugs if they do exist.

Diagnosis

The laboratory detection of malarial parasites in blood films still remains the most reliable method for the diagnosis of malaria. Advances in staining technic of thin and thick films have been directed toward obtaining a more speedy and satisfactory stain.

The basic technics, discussed previously,[1] continue to be used and relied upon. However the requirement of ten to forty-five minutes to obtain stains with various modified Giemsa technics was supplanted during the war by the more rapid Field stain.[29] More recently, another procedure, the J. S. B. stain, appears promising.[29, 30] The handicap to these methods lies in the fact that the stains are not available commercially. The stains for the solutions must be compounded in the laboratory by a combination of standardized stains, methylene blue and eosin. The Field stain, furthermore, is not so permanent as Giemsa's stain. The J. S. B. stain appears to be permanent, but insufficient time has elapsed since its development to be certain about its permanency.

An interesting colorimetric test for malaria has been devised that deserves further investigation and trials. Since serologic and other known tests for malaria fail too frequently during intervals between relapses and in latent malaria, Carlson, Mueller and Bissell[31] sought a new test. In recognition of the changed nature of the host's blood plasma during malaria and the known combining qualities of colloidal dyes with proteins, a test using dyes as indicators to detect the changes in plasma was devised. The test developed by these authors makes use of Congo red, quinine hydrochloride and the serum to be tested. The test gave positive results when tested against *P. knowlesi*, *P. gallinaceum* and *P. vivax* infections.

Immunity

During World War II, the seriousness of white people contracting malaria when going into malarious areas was greatly increased by the necessity of operations in the tropics. Immunity can be acquired to the disease by natives but only by constant infection or reinfection with local strains of parasites throughout life. The mechanism of acquiring immunity involving both antibody production and cellular defenses was reviewed previously, and the poor antigenicity of the parasites and the low protection of immune serum were discussed.[1] Few contributions have been made to alter the theories and interpretations expressed at that time. The advances, by necessity, have been concerned with practical serologic tests that could be used to detect quiescent malarial infections and characterize the strains of parasites encountered in diverse areas.

Relapsing tertian malaria contracted in the Mediterranean and Pacific theaters of World War II became a diagnostic problem of great importance. Since parasites cannot always be detected by laboratory methods during intervals between relapses, serologic tests, particularly the complement-fixation test, offered a possible solution to the difficulties.

In 1938 Coggeshall and Eaton[32] demonstrated the complement-fixation reaction for malaria. They showed that the reaction was group specific and that the simian and avian species of parasites could be used as antigens. The test subsequently was applied in the field to malaria in human beings by Dulaney and Stratman-Thomas[33] and Kligler and Yoeli.[34] This work was limited in extent, and during the war it became worth while to determine the value of the test in detecting *P. vivax* infections.

Extensive laboratory experimentation and field trials with the reaction produced a refined test that could be used with greater precision[29, 35–37] than originally. This new procedure failed to give the desired results in detecting the existence of relapsing malaria. The conclusion was reached that the test was still a supplementary rather than a dependable single diagnostic procedure. The work of Mayer and Heidelberger[38] showed that a single test with serum from a patient with suspected malaria was of value only if positive, but if negative, malaria could not be excluded. Furthermore, these authors make the following statement:

> The reaction diminished 1–6 weeks after relapses only to increase again shortly before or during or immediately after a subsequent relapse. Similar fluctuations may occur, however, without a clinical relapse rendering predictions hazardous.

These fluctuations occurred with a crude vivax antigen, or with normal red-cell stromata antigen.[39] The "soluble," more purified vivax antigen that Mayer and Heidelberger developed gave no such fluctuations, and it aided these workers in discovering for the first time a species specificity with complement-fixation methods. By the use of this "soluble" vivax antigen it was discovered that a positive complement-fixation test did not indicate the existence of protective immunity, since patients were observed who relapsed despite the detection of antibody in serum drawn shortly

before an attack. The results of Dulaney and Watson,[38] who used a "crude" antigen, further illustrate this point.

Heidelberger et al.[40, 41] also attempted to protect patients with relapsing vivax malaria by treatment with a homologous vaccine. These experiments were well controlled, and the relapse rate in the vaccinated groups was the same as that in the controlled groups. A further attempt was made by Heidelberger and his co-workers[42, 43] to vaccinate paretics against subsequent blood-borne infections and mosquito-borne infections with *P. vivax*. The patients, when infected with malaria three weeks after the last injection of vaccine, came down as usual with malaria; thus, no protection was obtained by vaccination. These very thorough studies verify previous results with animal malarial infections. For reasons unknown, the asexual stages of parasites appear to be very poor antigens. Freund et al.[44–46] were able to protect monkeys and ducks against malaria by using a vaccine containing asexual parasites, an adjuvant, emulsifying agent, and killed tubercle bacilli, but this method of vaccination has not been tried against malaria in human beings. Freund[47] reviews the theory and facts about this type of active immunization in a recent paper.

The development of false-positive tests for syphilis in patients with naturally acquired or artificially induced malaria has been the subject of extensive study. The need for clarifying the basic phenomena that cause positive syphilitic tests in patients having only malaria and for publicizing the occurrence among physicians became necessary to avoid placing under treatment for syphilis persons who do not have the disease. One book[48] and two review papers[49, 50] present the subject thoroughly. The results of a detailed study by Rein and Kent[51] of 7493 serums obtained at suitable intervals from 90 nonsyphilitic volunteers with naturally induced malaria are important. Some of the patients were studied as long as eighteen months. Each serum was subjected to a battery of 7 serodiagnostic tests for syphilis, and 44,958 tests were performed. Of the 90 infected subjects 57 (63.3 per cent) developed false-positive reactions with one or more tests during the course of the disease. The Hinton flocculation and microflocculation test employing a cardiolipin antigen yielded results of high specificity and the highest percentage of false-positive tests was obtained with the Kahn standard test. The results showed that false-positive tests for syphilis were highest in early primary malaria, lower in delayed primary attacks and lowest in relapses. Thus, any patient with a recent history of malaria or with a history of living in an endemic malarious area and a positive blood test for syphilis should have the existence of malarial infection ruled out before syphilitic treatment is instituted.

Physiologic Pathology

During World War II, malaria was an acute problem to the armed forces and personnel stationed in endemic areas. The problem involved not only the diagnosis and treatment of the clinical disease but also returning a man to full-time or limited duty or back to the United States from overseas. Later, after discharge from the services, the amount of disability to which a previous malarial patient was entitled had to be determined. Thus, criteria of radical cure and an investigation of physical and functional effects of the disease on the host had to be established. Too often misapprehension on the part of the patient was aided and abetted by the unfamiliarity of the physicians with the course and results of the infection.

As a result of experimental and field trials, quinacrine (synonyms, atabrine and mepacrine) was found to be a true causal prophylactic and a radical cure for infection with the malignant tertian parasite *P. falciparum*. The majority of the problems resulting from malarial infection had to do, then, with relapsing tertian malaria. Several investigations were conducted by the Army and Navy to discover the organic and the psychologic causes for morbidity produced by *P. vivax*. These investigations were very thorough, they were conducted independently of each other, and the results add greatly to knowledge of the course of this infection and the sequelae from the disease. These results are of distinct value in determining procedures concerned with the disability granted by the Veteran's Administration to persons who previously had an infection with malaria.

In the first study of Tumulty et al.,[52] 50 soldiers who had suffered recurrent attacks of benign tertian malaria were selected. These soldiers were subjected to a long period of functional, metabolic and psychiatric tests. The evaluation of each soldier and his physical and mental condition was extended over a period of seven days. The procedures are not mentioned in detail, but they included a complete history and physical examination, basal metabolic rate, liver-function test, neurologic test, clinical pathologic test, hematologic test, stool examinations for ova and parasites and serologic test for syphilis.

It is impossible to give in detail the methods of testing used in this study and the very careful evaluation and interpretation of the results. The 50 patients revealed no evidence of damage or dysfunction of the organic systems measurable by the technics employed. The authors believed that the absence of such organic changes was the result of the fact that these patients were treated adequately and early in their attack. However, weight loss, weakness and debility in varying degrees were present in all but a very few of the pa-

tients. The chronic symptomatology found in these soldiers was believed to be caused primarily by malaria. However, the way the patient adjusted himself to the disease and the environmental factors present at the time of illness were believed to contribute greatly to the development of the symptoms.

A second series of studies by Bianco et al.[53] differs from those of Tumulty in the fact that they extended over a period of twenty-six months. During this time 1500 attacks of malaria were observed, and the persons studied were tested in ways that coincided in some cases with the tests used by Tumulty and his associates but differed in other respects.

All the men examined in this study were either Marine or Navy personnel. One third of the men had recently returned from overseas duty, and two thirds had been back in this country two to eighteen months without having had intervening quinacrine therapy. It is important to note that these authors refused to admit a patient to their study without first having found definite malarial parasites to establish the diagnosis of malaria. It was found that the information given by the patient and the available history were unreliable in many cases, and thus competent technicians were used to arrive at the diagnosis of malaria in the presence of fever and with or without an enlarged spleen. The technicians never failed to find parasites in the peripheral blood within seventy-two hours when thick smears were examined at eight-hour intervals. It should be noted further that parasitemia was commonly of low density, revealing itself, however, during the first few days of clinical malaria. The blood-smear technic was of no value if the patient had taken antimalarial drugs several days previously or if a clinician had prescribed sulfonamides to the patient, thinking that fever was due to another infectious agent.

Some of the findings that these authors report include the absence of the chronically enlarged spleen, although the spleen in a number of cases was palpable during an attack of acute malaria. Leukopenia was fairly common. The erythrocyte sedimentation rate was increased in 68.9 per cent of the cases during the acute attack, and in 16.3 per cent during the remission stage of the disease. The icteric index was also increased during an acute attack. Some of the complement-fixation tests failed to show any relation between parasitemia and the development of subsequent relapse. The results with the serologic tests for syphilis were as follows: a variety of tests or methods of testing were used, and the authors found that in a more or less random sample of serum from patients taken during clinical malaria and between attacks, about 90 per cent of the results were negative. Positive reactions increased during the second and third weeks after the onset of clinical malaria, but the serum became negative in most cases within four weeks and in all cases within ten weeks after onset. The importance of these tests is included in the statement that 20 to 30 per cent of the cases gave positive reactions by one or more of the tests used two to three weeks after the onset of clinical malaria. Positive tests, however, were almost never found later than four to six weeks after onset.

The attempt on the part of Bianco and his collaborators to pin down the exact mechanism underlying malaria relapses is worth commenting upon. Their purpose, in part, was to allay the fears of many medical and lay personnel that "South Pacific" malaria meant a long if not permanent disability. Studies on the relapses and associated symptoms, length of time between relapses, precipitating causes and reactions to treatment led to the following conclusions. "With the passage of time away from highly endemic areas, the frequency and severity of relapses shows an unmistakable trend toward the eradication of the malaria within 3 years by development of immunity in the host." Furthermore, they state that "many of the alleged postmalarial sequelae bear no relation to malaria *per se*, but are rather directly related to the personality of the individual."

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 34271

PRESENTATION OF CASE

A fifty-eight-year-old unmarried woman, a floral designer, entered the hospital complaining of abnormal vaginal bleeding.

The patient underwent a normal menopause ten years before entry. Her periods prior to that time had always been regular. Since the menopause she had had no vaginal bleeding until six weeks before entry. At that time she noted enough bloody staining to require the wearing of a pad. This bleeding recurred every three or four days until three weeks before entry, when the bleeding occurred almost every day. It was never profuse, was not accompanied by pain and was otherwise asymptomatic. She had lost no weight. Two weeks before entry a vaginal smear was reported negative.

The family history and past history and a review of the systems were noncontributory.

Physical examination showed a well developed, well hydrated, obese woman. The heart was slightly enlarged, the border of cardiac dullness extending to the left. The blood pressure was 150 systolic, 95 diastolic. In the abdomen was a movable, nontender mass arising from the pelvis and extending to the level of the umbilicus. Vaginal examination revealed the presence of old blood. The cervix itself was clear. Rectovaginal examination disclosed a large mass filling the pelvis, rising nearly to the navel. It was more prominent on the left and could be moved somewhat. Movement of the mass produced motion of the cervix, and the two seemed to be connected.

The urine was normal, and the hemoglobin was 13.6 gm.

On the day after entry an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WARD I. GREGG: In this fifty-eight-year-old unmarried woman, whose periods were always regular and who had lost no weight, bleeding had been active for three weeks but present off and on for six weeks.

The causes of postmenopausal bleeding ten years after the menopause I will name and discuss as we go along. The most common cause occurring in 50 per cent of postmenopausal bleeders is adenocarcinoma of the fundal portion of the uterus. Today the next most frequently observed cause — but perhaps in this case not quite so important — is the use or misuse of various estrogens for menopausal symptoms. Proliferation or even hyperplastic endometrium can be produced by continued ingestion of estrin at any age. In this case, however, ten years with no mention of menopausal symptoms is rather late for symptoms to develop. We can forget about that.

To proceed to the findings on physical examination, the patient had a large pelvic mass, which extended up above the pelvic brim almost to the umbilicus and was consistently felt as one mass. We have all examined women and found that one mass may actually consist of a number of adherent masses over the uterus. For the purpose of this discussion we should consider this one mass connected with the cervix and assume that it was the uterus. It was a large uterus, and the next possible diagnosis is therefore a degenerated fibroid. This is apparently rare unless it was a submucous fibroid in which ulceration had occurred. Another possibility that we see from time to time is a polyp, either endocervical or endometrial. Polyps sometimes ulcerate, bleed and produce symptoms similar to those in the case under discussion. Ten years after the menopause is a short period for atrophic vaginitis. Also, the bleeding of atrophic vaginitis rarely becomes constant like that which occurred during the first three weeks of this woman's illness. Carcinoma of the ovary, with bleeding as the primary symptom, is rare unless it has invaded the endometrium. The same statement is true of carcinoma of the Fallopian tube, in which bleeding occurs very rarely until the carcinoma has penetrated the endometrium by way of the tube. It is a possibility but not likely. A year ago a patient was presented to me with an almost identical history, and she had a carcinoma of the Fallopian tube.

I think probably the point of greatest significance here is the fact that two weeks before entry a vaginal smear was reported negative. One vaginal smear, if positive, may mean that the patient has an endometrial carcinoma. However, in the experience of the Vincent Laboratory 23 per cent of proved adenocarcinomas of the endometrium have had negative smears. Scheffey et al.[1] in Philadelphia, have found 40 to 50 per cent of proved adenocarcinomas with negative smears. A negative smear does not rule out completely the possibility of adenocarcinoma. The frequency with which fibroids appear along with carcinoma of the fundus runs in the neighborhood of 33 per cent. The rather scanty bleeding in this particular case may point toward a small, early lesion. But an advanced carcinoma may break down late. The other thing of importance is that this patient was an unmarried woman, and it has been shown in various series that adenocarcinoma is more likely to develop in nulliparous women who have been exposed to long, uninterrupted estrogen levels. The same group of people usually have dysfunctional bleeding with anovulatory cycles at the climacteric. Randall[2] pointed out in his series that about 45 per cent of postmenopausal adenocarcinomas occurred in women who had dysfunctional bleeding at the time of the climacteric, although the carcinoma was not evident until years afterward. I therefore have a strong feeling that this patient had a uterine fibroid and adenocarcinoma of the endometrium.

Clinical Diagnosis

Ovarian cyst?
Degenerating fibroid uterus?

Dr. Gregg's Diagnosis

Adenocarcinoma of the uterus, with uterine fibroid.

Anatomical Diagnoses

Adenoacanthoma of fundus of uterus.
Follicle cyst of ovary.
Uterine leiomyomas.

Pathological Discussion

Dr. W. Philip Giddings: Dr. Arthur W. Allen thought that the mass, of which, as I recall it, the patient was not aware, represented ovarian disease of some type. She was operated on with a diagnosis of ovarian cyst. Prior to laparotomy a curettage was performed, and grossly carcinomatous material was obtained. At laparotomy a slightly enlarged uterus and a large cyst of the ovary, arising on the left side, were removed.

Dr. Benjamin Castleman: Although the large mass that was felt was an ovarian cyst, there was, in addition, a uterine fibroid 2 cm. in diameter. I do not believe that it had much to do with the adenocarcinoma that was located in the fundus. In a few areas the cancer showed some squamous-cell metaplasia, making it an adenoacanthoma. The ovarian cyst was smooth, both inside and out, and perfectly benign.

Dr. Howard Ulfelder: It would be interesting to know if the vaginal smear showed estrogen effect. In a woman of this age estrogen effect in a vaginal smear is found much more frequently in women with adenocarcinoma of the fundus.

Dr. Gregg: Along with that there is another point that comes up. An estrogen effect in a vaginal smear can occur with granulosal-cell tumor of the ovary. A granulosal-cell carcinoma of the ovary

and an adenocarcinoma of the endometrium are frequently found together and could be caused by the constant estrogen stimulation. I do not believe that the amount of bleeding or the duration indicate such an effect in the case under discussion.

DR. CASTLEMAN: The endometrium away from the carcinoma was of the atrophic senile cystic type, which some people believe is a precursor of adenocarcinoma.

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CASE 34272

PRESENTATION OF CASE

A twenty-seven-year-old housewife entered the hospital complaining of an itching rash.

Two years before entry, about three months after the birth of her first and only child, the patient developed itching lesions on the left ankle. These gradually spread until a pruritic dermatitis involved the legs, arms and trunk, and even spread to the face and scalp. A slight remission of the dermatitis was noted on two occasions, lasting for several weeks, but each time the dermatitis returned as before. She had been seen by many physicians and had had a variety of treatments, including allergy tests, antihistamines, local applications and x-ray therapy to localized skin areas, all with little or no effect. Four months prior to admission the patient was given penicillin tablets by mouth for the appearance of some enlarged cervical lymph nodes. One week after the penicillin was discontinued she developed a generalized urticaria, and she had repeated attacks of urticaria up until the time of admission.

Physical examination revealed a moderately well developed and well nourished young woman, who was nervous and emotionally upset because of fatigue, itching and worry. Several small firm nontender lymph nodes were palpable along the anterior border of the sternocleidomastoid muscle and above the clavicle, measuring up to 2 cm. in diameter. The skin findings were those of an urticaria with multiple excoriations on the flexor surfaces of the arms and over the scapulas, lower back and buttocks. Similar but less marked lesions were present on all other parts of the body. The rest of the examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a hemoglobin of 13.2 gm. and a white-cell count of 7700, with 49 per cent neutrophils, 24 per cent lymphocytes, 5 per cent monocytes, 19 per cent eosinophils and 2 per cent basophils. A blood smear showed only a slight increase in the number of platelets. The urine was normal. A stool was guaiac negative, and no parasites or ova were found. The total serum protein was 6.90 gm. per 100 cc., with 4.83 gm. of albumin and 2.07 gm. of globulin. The nonprotein nitrogen was 25 mg., the blood cholesterol 125 mg., the serum calcium 9.9 mg., and the phosphorus 5.4 mg. per 100 cc. The alkaline phosphatase was 1.9 units per 100 cc.

A basal metabolic rate was +20 per cent. A chest film showed a rounded mass of increased density measuring approximately 6 by 7 by 9 cm. in size, occupying the upper anterior mediastinum. The trachea was deviated to the left and somewhat posteriorly. The mass was smooth in outline. It did not appear to have caused any embarrassment to the aeration of the lungs. The lung fields were clear, the heart was normal in contour, the diaphragm was normal in position, and the chest cage was not remarkable. Tuberculin skin tests in dilutions of 1:10,000, 1:1,000 and 1:100 were negative. A repeat basal metabolic rate was +17 per cent. A cervical lymph node was biopsied and showed chronic inflammation. X-ray studies of the bones of the hands and feet showed no osteoporosis or osteolytic lesions. During the first two weeks in the hospital the dermatitis subsided until only a few lesions persisted on the forearms. During this period the temperature, pulse and respirations had always been normal.

On the seventeenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LOWREY F. DAVENPORT: The only complaint in this case was the persistent itching for a period of two years, with few or no constitutional symptoms. The objective findings are the changes in the differential count, the eosinophil count going as high as 19 per cent, the enlarged lymph nodes and the mass in the chest. In trying to arrive at a diagnosis it might be well at this point to review the x-ray films.

DR. JAMES J. MCCORT: These films were taken at the time of admission — a posteroanterior chest film, a grid film and a film of the hands. The large mass is present in the anterosuperior mediastinum, extending mostly to the right, but one can see a portion of it on the left. On the lateral film it is seen to be anterior to the trachea and has displaced this structure slightly posteriorly and to the left. There are no enlarged lymph nodes in the perihilar region. Both lungs are clear. The heart and vessels are normal. The mass is quite smooth and shows no calcification.

DR. DAVENPORT: We have to decide immediately whether or not the symptom of pruritus over two years was a manifestation of a general systemic disease, or whether it was an incidental complaint and entirely unrelated to the mass in the chest. I

gather from the history that during this two-year period the patient had no symptoms referable to the chest, and her chief complaint was from the itching lesion in the skin. The abstract speaks of pruritic lesions. Pruritus, as I understand it, is a symptom — itching of the skin — without any visible change in the skin itself. It would make some difference whether there actually was a skin lesion present, or whether it was pruritus with secondary changes due to scratching.

Dr. Jacob H. Swartz: When I first saw this patient she complained of generalized itching. The predominating lesions were not urticarial as stated in the record but rather excoriations, lichenification and pigmentation, with few urticarial wheals. Most of the cutaneous manifestations were secondary to scratching, although some of the lesions may have been primary and produced itching in this particular case.

Dr. Davenport: We have to consider for the purposes of discussion the possibility that the itching was not connected with the general picture. I do not need to discuss some of the remote possibilities in the differential diagnosis. If, however, these skin lesions and the primary complaint of itching had nothing to do with the general picture as found, we must consider what could cause a symptomless mass in the anterior mediastinum. We can only go on a percentage basis in the differential diagnosis of such a mass. We have found in the past in young people that in the anterior mediastinum teratoma and dermoid cyst were more common, and neurofibromas were much more common in the posterior portion of the chest. If we assume that the fundamental difficulty was a skin lesion, we should consider such primary skin disturbances as mycosis fungoides, in which, in an occasional case, general changes throughout the body are described. It can affect various internal organs but would not explain satisfactorily this entire picture with a mass such as that seen in the x-ray film, the blood findings, the pruritus and the skin lesions.

For the purpose of differential diagnosis I believe we need discuss only two conditions: Hodgkin's disease and sarcoidosis. Hodgkin's disease is a disease of young age groups. It can cause masses of varying sizes in any of the lymph structures. It quite commonly affects the cervical lymph nodes. It can cause marked enlargement of the nodes in the mediastinum and of the hilar nodes. It can be accompanied by pruritus. As I understand it, the itching that accompanies Hodgkin's disease is in a true sense pruritus, and rarely are definite lesions in the skin associated with this condition. Hodgkin's disease, as I have said, is more common in younger age groups, and this woman was in the third decade. However, on a percentage basis, it affects males more than females. The fact that she was a woman is of no real diagnostic significance. Although a patient with Hodgkin's disease may have a perfectly normal blood picture, quite commonly there is a slight increase in the leukocytes, and in many cases there is an eosinophilia. The pruritus in Hodgkin's disease may be a premonitory symptom and has been described as going on for months or even years before the development of signs of disease elsewhere. Hodgkin's disease, therefore, could explain everything that has been found in this patient.

Another condition that we see more and more frequently that can produce these changes is sarcoid disease. Sarcoidosis can attack at any age but is more common in young people. It is occasionally a disease with pruritic manifestations. It can and frequently does occur without any symptoms at all. Skin lesions do occur in sarcoid and they are described as elevated, dusky, indurated lesions that, I assume, are at times quite easily confused with urticaria. Itching of such lesions has been described as a distressing and continued symptom throughout the early course of the disease. Sarcoid involvement of the lymph nodes is quite common, and it can involve any organ of the body. Involvement of the hilar nodes is not uncommon. Most cases of sarcoid show a more diffuse involvement of the hilar structures than was present in the case under discussion. The involvement is usually symmetrical in distribution, and the process is apt to spread into the lung itself through a peribronchial pattern. Occasionally, it produces lasting fibrosis with permanent changes in the lung, but many cases have cleared up completely without any visible changes remaining in the x-ray films of the chest.

This scrapbasket of sarcoid is puzzling, and differential diagnosis is difficult. In the absence of histologic evidence we have to reason from negative data. Here is a patient who for two years had a generalized disease, and yet when she came to the hospital the only real complaint was itching. I know of no other situation that could cause such diffuse changes throughout the entire body and cause so few constitutional symptoms as sarcoid. Also, although I do not believe the decision is difficult in this case, we often must distinguish between tuberculosis and sarcoid. We frequently rely on the observation that the tuberculin test in probably 90 per cent of cases of sarcoid is negative. It is recognized, however, that perhaps 10 per cent of cases of proved sarcoid have a positive tuberculin test.

In trying to evaluate the significance of a positive or negative tuberculin test in a twenty-seven-year-old housewife, it would be of some interest to know whether the patient was born with a family background of tuberculosis or where she had lived. A negative tuberculin test through all its dilutions in a twenty-seven-year-old city dweller would be of definite diagnostic significance.

A Physician: The patient was born and brought up in New York City.

Dr. Davenport: Unfortunately, the tuberculin test is becoming less and less of a diagnostic aid because the incidence of tuberculosis throughout the country is dropping. In the Midwest there are several counties where no children in the schools show a positive tuberculin test. Here in Massachusetts the figures vary from 40 to 45 per cent in urban high schools to 15 per cent in suburbs such as Newton. This finding of a negative tuberculin test in a woman of twenty-seven, born and brought up in New York City, may be of definite diagnostic importance. We have, in sarcoidosis, a granulomatous disease that can cause skin lesions, severe and continued pruritus, enlargement of the lymph nodes and bizarre changes in the chest. It is a disease that is frequently accompanied by mild leukopenia with occasionally a definite eosinophilia such as that reported in this case.

I believe that the final diagnosis comes down to two granulomatous diseases, Hodgkin's disease and sarcoid. I cannot believe that this person had extensive Hodgkin's disease involving so much of the body with so few constitutional symptoms. A negative biopsy in sarcoid would be less surprising than a negative biopsy in a case of Hodgkin's disease. I should then make as my diagnosis Boeck's sarcoid disease, involving the skin, with a rather unusual involvement of the mediastinal lymph nodes.

Dr. Donald S. King: I saw this patient in consultation. I got off on the wrong track and was inclined to say that the skin lesions and enlarged lymph nodes were a separate condition from the asymmetrical chest lesion. Not having seen an itching sarcoid case, somehow sarcoid did not make much impression on my mind and I tried to bring in a benign tumor of the chest in this locality as an entirely separate condition from the skin and lymph nodes. I was influenced a great deal by the negative biopsy of the nodes. My preoperative guess was bronchiogenic cyst and then dermoid or teratoma.

Dr. Swartz: I thought this case served as a good example to emphasize the close relation between dermatology and internal medicine. When the patient was first seen a provisional diagnosis of lymphoma was made because of a nonspecific eruption with severe pruritus accompanied by enlarged and hard lymph nodes in the supraclavicular areas, axillas and groins. This woman had the type of eruption seen in Hodgkin's disease: urticarial, morbilliform, scarlatiniform and zosteriform. Goldman,* in 1940, reported 212 proved cases of Hodgkin's disease with cutaneous manifestations in 38 per cent. The predominant manifestations were urticaria, pigmentation and excoriations with severe itching. This patient had these symptoms in addition to the presence of adenopathy. The chest film further confirmed the possibility of lymphoma, although the other diagnoses mentioned by Drs. Davenport and King could not be ruled out without surgery.

In the presence of a nonspecific eruption I was taught to consider the following possibilities: drug eruption, blood dyscrasia, the lymphoma group, subclinical jaundice or some other systemic disease. The psychogenic factor should be considered only when the above-mentioned conditions had been ruled out. This is well exemplified in this case. This patient was treated for two years for pruritus of psychogenic origin. We recently had a case of generalized pruritus that showed only excoriations and icteric discoloration of the scleras. The diagnosis to date is carcinoma of the head of the pancreas. Systemic disease as a cause of pruritus without specific lesions should always be considered.

Sarcoid lesions of the skin look much different from those that this patient presented and are usually nonpruritic. They are infiltrated. Excoriations are absent as a rule. Dr. Davenport did not have the benefit of seeing the lesions that this patient presented. I am certain that he would have excluded sarcoid if he had had the opportunity to examine the patient's skin.

Dr. Bernard M. Jacobson: On a medical consultation I considered all the possibilities mentioned so far. I also got off on the wrong track because of the two-year duration of symptoms of itching in a healthy-looking girl.

Clinical Diagnosis

Bronchiogenic cyst?
Lymphoma?

Dr. Davenport's Diagnosis

Sarcoidosis.

Anatomical Diagnosis

Malignant lymphoma, Hodgkin's type.

Pathological Discussion

Dr. Tracy B. Mallory: An attempt was made to establish the diagnosis by biopsy of a cervical lymph node. That proved fruitless. A group of three small nodes was removed, and they showed only nonspecific, mild lymphoid hyperplasia. Therefore, it was decided that it was justifiable to explore the mediastinal mass, hoping that it might be a tumor that was resectable. The patient was operated on by Dr. Richard H. Sweet, who found a large tumor lying mostly between the trachea and the superior vena cava. It partially encircled the latter, and although he was able to remove most of the tumor, he could not get all of it. Histologic examination showed a characteristic Hodgkin's disease full of large Reed–Sternberg cells, the largest I have ever seen. There was considerable fibrosis and some tissue infiltration with eosinophils.

*Goldman, L. B. Hodgkin's disease: analysis of 212 cases. *J. A. M. A.* 114:1611-1616, 1940.

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ECONOMIC PROBLEMS OF THE VOLUNTARY HOSPITAL

FIFTEEN years ago, during the height of the depression, voluntary hospitals were confronted with a most critical situation. Private and semiprivate beds were unoccupied; public wards were overcrowded. Philanthropic support was materially affected by general economic conditions, and the voluntary hospitals found themselves in dire straits indeed. As conditions improved, private and semiprivate facilities became increasingly occupied, a fact that demonstrated a willingness on the part of the American public to pay its way in accordance with its financial means.

Today, the voluntary hospital is confronted with an even more critical situation, despite the fact that hospitals in general are overcrowded as never before, and beds of all types, including private, semiprivate and ward, are in great demand. Hospital income has increased to its highest peak, and yet these institutions are confronted with the largest deficits in their history.

The most important factor in the development of this situation is that operating costs have practically doubled within five years, salaries and wages representing the most substantial factor in the tremendous increase in the per diem cost, with the cost of supplies a close second.

The solution of this problem will be difficult, but it will be found. If the advantages of hospital care are to continue to be available and if the scientific measures that play a part in these increased costs are to continue to be applied, little can be done to reduce expenditures. The answer, therefore, must be found in opportunities for increasing hospital operating income, particularly for the care of patients in need of financial assistance for the payment of the hospital bill.

This brings into focus the importance of reimbursement on the basis of costs from all who are able to pay. It emphasizes the wisdom of insurance protection to meet the expenditures of frequently unpredictable illness. It emphasizes the need for the recognition on the part of governmental agencies of their obligation to reimburse the voluntary hospital on the basis of costs, particularly for those who are considered a public responsibility.

It should be agreed that the voluntary hospital, which concerns itself not only with the care of the sick but also with the training of personnel, the conduct of research and the prevention of disease, is worthy of the increasing and continuing support of everyone in the community who is in a position to give financial assistance.

From the point of view of the patient served, the medical profession should exercise good judgment in limiting admission to patients who are actually in need of "in-bed" care. To hospitalize a person because he is a member of Blue Cross, or even because he can afford to pay for service, is uneconomic, unsound and particularly unwise in that it deprives someone in more urgent need of the opportunity for medical or surgical treatment.

Equally important is the employment of only those diagnostic procedures and therapeutic measures that are essential for diagnosis and treatment. This will save time and money and will play a part in the more regular utilization of a hospital bed.

TROPICAL DISEASES IN NEW ENGLAND

Tropical diseases occasionally invade temperate zones, and the possibility of their occurrence in New England deserves greater emphasis. The report of 2 cases of yaws in this issue of the *Journal* and the recent report of 2 cases of creeping eruption (*Larva migrans*)* lend added weight to the possibility. Another very recent case of *Larva migrans* infection in a person returning from East Africa, as yet unpublished, further confirms the responsibility of the physician in the matter of tropical disease in New England. These particular diseases are infections that have skin manifestations; they usually occur in warm climates, but the return of military personnel and others from war duty and the rapidity of modern air transportation have increased the risk of transferring to the population of this country certain of the cutaneous diseases, as well as other general diseases, ordinarily found in the tropics. The greater volume of travel since the war in the countries to the south of the United States provides additional opportunities for contracting diseases that are endemic in those countries. Tropical and semitropical diseases have been observed with increased frequency along the southern borders, although in the northern third of the country such diseases are still relatively infrequent.

Parasitic diseases of the tropics due to both animal and vegetable parasites and the diseases of bacterial origin, with their complications, will need to be considered in differential diagnosis for some time to come by physicians throughout this area. A carefully taken history, including data about any change of abode or travel, in cases of unusual skin eruptions may be of considerable importance in furnishing a clue to the interpretation of any such manifestation. In the differential diagnosis of granulomatous lesions and of some of the curious eruptions, thought must be given to the possibility of a tropical factor as a causative agent. Moreover, the occasional appearance in this general area of such infections as actinomycosis, blastomycosis, sporotrichosis and tularemia renders it advisable for physicians to be alert to the possibility of these unusual diseases as well.

*Lowe, C. U., and Augustine, D. L. Creeping eruption in New England: report of two cases. *New Eng. J. Med.* **236**:658-661, 1947.

RAW MILK AND Q FEVER

Several times in the past few years attention has been called in these columns to the disease Q fever. At first, this was considered to be an influenza-like disease indigenous to some parts of Australia, where it affected mostly dairy workers and foresters. Interest in the disease in this country was first aroused by the isolation of a rickettsial agent that was identical with *Rickettsia burneti*, the causative agent of Q fever from ticks in many parts of western and southwestern United States, and by the occurrence of occasional cases of infections produced by this agent in Montana.

The first significant infections in this country, however, were observed during an outbreak of laboratory infections at the National Institute of Health in which a rather severe type of atypical pneumonia simulating the viral pneumonias constituted an important part of the clinical picture of the disease. Since that time strains of Q fever have been recognized as the cause of Balkan grippe, of several explosive outbreaks of infections among British and American troops in Italy and the Balkans, and also of additional laboratory outbreaks. In this country circumscribed epidemics of Q fever have been recognized among stockyard and packinghouse workers in Amarillo, Texas, and in Chicago, and serologic evidence of previous infection with this disease among packinghouse workers has recently been uncovered in Fort Worth, Texas.[1]

The most recent findings of interest in this disease have been the occurrence of a number of proved cases of Q fever in the region of Los Angeles, California, and, what is more important, the isolation of the causative rickettsial agent from raw milk in at least four dairies in this region.[2] The isolations of these rickettsias were made from samples of milk studied

in three separate laboratories — the Q Fever Laboratory in Los Angeles, the National Institute of Health in Bethesda, Maryland, and the Rocky Mountain Laboratory in Hamilton, Montana.

Although the rickettsias were recovered from raw milk, the available epidemiologic evidence did not indicate that the drinking of milk was the cause of the majority of the cases that have been studied thus far. However, it was believed by Huebner and his co-workers[2] that infected milk may serve as a source of infection by some mode as yet undetermined. Proximity to dairies by reason of occupation or residency was a common factor in the histories of more than 50 per cent of the cases in the Los Angeles area. Except for the dairy workers, however, the infected persons rarely used milk from the nearby dairies. Fairly extensive surveys, on the other hand, have revealed that from 10 to 20 per cent of the dairy cows in the Los Angeles area possessed serum antibodies for Q fever, which is strong presumptive evidence of recent infection of these animals with the rickettsia.

The relative ease with which *R. burneti* was recovered from milk in the Los Angeles dairies suggests a high degree of availability of this pathogenic agent to the human and animal population of that area, since nearly all that milk is transported about the county before processing and much of it is sold raw. The facts that Q-fever infection has been demonstrated in the human population and that a source of the rickettsias of this disease was found to be widely disseminated in the same area suggest a causal relation.

The data, however, do not prove definitely whether or not milk represents an effective source of infection to man. In the outbreaks among packinghouse and stockyard workers and also in some of the laboratory infections a pulmonary route of infection was considered most likely. The same fact may also have been true in outbreaks among troops in the Balkans.

Of additional interest are the studies of a limited number of cows that were shedding *R. burneti* in their milk. These studies failed to yield the rickettsial agent from whole blood, blood clots, urine or feces. Such findings and the absence of a demonstrable illness in the infected animals suggested that a local infection of the udder occurs in the absence of concurrent infection in the cow. Furthermore, the presence of these rickettsias was not associated with any observable disease in the udder or with diminution in either the quality or the quantity of the milk. There seems to be no way other than isolation of the rickettsia for recognizing the animals that shed the rickettsia in their milk.

Preliminary studies of the methods of pasteurization of the milk, as practiced in at least two of the large milk plants in the Los Angeles area, indicated that these procedures rendered the naturally infected milk apparently noninfectious, at least for guinea pigs. The residents of Los Angeles will therefore have another potent argument for insisting on pasteurization of their milk.

References

1. Strauss, E., and Sulkin, S.E. Studies on Q fever: complement-fixing antibodies in meat packers at Fort Worth, Texas. *Proc. Soc. Exper. Biol. & Med.* **67**:139-141, 1948.
2. Huebner, R. J., Jellison, W. L., Beck, M. D., Parker, R. R., and Shepard, C. C. Q fever studies in southern California: I. Recovery of *Rickettsia burneti* from raw milk. *Pub. Health Rep.* **63**:214-222, 1948.

ON SECOND THOUGHT

Congress, on second thought, has reversed its decision to consign the World Health Organization to limbo. The terms on which Uncle Sam is willing to play with the other boys are even being softened. Thus, the House provision that the United States member of the Organization's executive board must have had at least ten years in "active practice" has been reduced to three years' experience in the treatment of patients.

The House has also discarded its insistence that every employee and attaché of this country's delegation must be approved by the Secretary of State. The Senate, not to be outdone in graciousness, has allowed withdrawal notice to be lengthened to a year, instead of the ninety days originally insisted upon by that august body.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

Crotty — Martin F. Crotty, M.D., of Cambridge, died on June 5. He was in his fifty-sixth year.

Dr. Crotty received his degree from Boston University School of Medicine in 1924. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American Medical Association.

His widow survives.

MEDICOLEGAL ABSTRACT

Hospitals — Dismissal of nurse at request of physician. In a recent Massachusetts case a registered nurse complained that a doctor had improperly induced a hospital to suspend her right to work at the hospital. There was testimony that it was a valuable business relation for the nurse to have her name on the hospital's call list of nurses and to have the privilege of nursing at the hospital and that the relation afforded her fairly reliable means of access to employment in her profession. The court held that unless the doctor was privileged for some reason he would be liable to a nurse under these circumstances for the harm caused her if he was responsible for her suspension from the hospital. Obviously, a doctor may not obtain a nurse's dismissal solely out of malice or for capricious reasons and without justification.

In this case, however, there was testimony, which the jury may have disbelieved, that a patient of the defendant had told him that the plaintiff had made derogatory remarks about him. These remarks were that he thought he and his patients were the only ones that counted and that he was "a two-cent doctor" and did not know how to take care of his patients. There was also testimony that the defendant had been told that the plaintiff had attempted to take for her patient some bed linen and a blanket intended for the defendant's patient.

Other than the words of the Nightingale Pledge, "With loyalty I will endeavor to aid the physician in his work and devote myself to the welfare of those committed to my care," it appeared that there were no regulations concerning the conduct of the nurses. Their supervision was part of the general administrative duty of the board of management. It was substantially agreed, however, that for a nurse to criticize a doctor to his patient would be a breach of ethics.

The plaintiff testified in effect that she had not made the derogatory remarks about the doctor, that on a prior occasion he had threatened to have her taken off the registry and that the superintendent of the hospital had told her that her name had been taken off the list since he was a very important person in the hospital. The defendant himself contradicted this and testified that he had simply reported to the hospital superintendent what his patient had told him about the conduct and language of the plaintiff, which in his opinion was a breach of ethics, and that he did not request the superintendent to omit the plaintiff or to take her name off the list, but that the superintendent had acted on her own initiative. Both the defendant and the superintendent admitted that the plaintiff was otherwise competent as a nurse and that she would not have been restored to the list until she had seen the defendant.

These conflicts of testimony were for the jury, which found for the plaintiff, to resolve, but in the course of its opinion the court made some interesting remarks about the type of case in which a doctor might be privileged in causing a nurse's dismissal. The court said:

> We assume that if the plaintiff did disparage the defendant to his own patient a privileged occasion would arise which would justify the defendant in doing something in relation to the matter for the purpose of maintaining the necessary discipline in the hospital and efficient working relations between nurses and physicians. A privileged occasion of some sort might perhaps arise if the defendant had been credibly informed and believed that the plaintiff had made the statements attributed to her, even if in fact she had not made them. We do not decide these questions.

In any question of privilege the issue is not only whether the doctor was privileged to do what he did but also whether he was privileged to do it as he did. Even assuming that a nurse actually made derogatory statements, the caution of the court's opinion intimates that the doctor's action must be taken "for the purpose of maintaining discipline in the hospital and efficient working relations," and not for the purpose merely of injuring the nurse in her profession, which the jury apparently found was his purpose here, or for other purposes unrelated to the privilege. However, the court thought it unnecessary to consider whether, if the defendant had a privilege of some kind, he exceeded its limits in what he did, or whether the jury could find that he lost any privilege by resort to improper means or that he was so far actuated by express malice that all privilege ceased. (*O* — v. *W* —, 1948 *Mass. Adv. Sheets.* 193.)

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

STUDY OF HEART DISEASE IN MASSACHUSETTS

A public-health heart-disease program sponsored jointly by the local boards of health, the Massachusetts Department of Public Health and the United States Public Health Service was endorsed by the Council of the Massachusetts Medical Society at its last meeting. This study is being conducted in an effort to reduce the morbidity and mortality from heart disease in adults, particularly in the productive years. Funds and personnel will be provided by the United States Public Health Service.

The projects have also been endorsed in principle by the New England Heart Association. A technical advisory committee appointed by Dr. Vlado A. Getting, commissioner of Public Health, includes Dr. Howard B. Sprague, chairman, Dr. Edward F. Bland, Dr. Laurence B. Ellis, Dr. James M. Faulkner, Dr. Burton E. Hamilton, Dr. Hugh R. Leavell, Dr. Samuel A. Levine, Dr. Benedict F. Massell, Dr. Loren D. Moore, Dr. Samuel H.

Proger and Dr. David D. Rutstein. The epidemiologic study of heart disease will be conducted in Framingham in co-operation with the Department of Preventive Medicine of the Harvard Medical School and the Framingham Board of Health with the following objectives: to devise and evaluate a method for mass survey of a population for heart disease; to examine a suitable sample of the population to determine the prevalence ratios of various forms of heart disease in the adult groups between twenty and seventy years of age in this area; to carry out a follow-up study to determine the rate at which new cases occur in the population as it ages — that is, the risk of attack — and to observe the natural course of certain forms of cardiovascular disorders; to determine if possible through analysis of data collected the relation of factors such as those of race, heredity, occupation, body build, use of stimulants and diet to the development of heart disease; and to collect records for evaluation of instruments, such as the electrokymograph and photofluorograph as case-finding tools.

A local professional advisory committee, consisting of T. J. Carnicelli, M.D., Hugh Folsom, M.D., H. M. Levenson, M.D., E. J. DeNicolais, M.D., J. H. McCann, M.D., C. M. Bonzey, Jr., M.D., H. G. Murray, M.D., M. B. Strauss, M.D., P. B. LeBaron, D.M.D. and Mervin Weitz, D.M.D., will assist in guiding the Framingham program.

The heart-demonstration program will be conducted in Newton as a co-operative project with the Newton Health Department, under the immediate supervision of Dr. Ernest M. Morris, director of public health, with the following objectives: to plan and develop in co-operation with the local medical profession and other agencies concerned a public-health program to help meet the increasing problem of heart-disease morbidity and mortality, especially in the productive ages; to prepare a basic manual with information for workers in a public health heart program (the writing of the manual will be supervised and edited by the Technical Advisory Committee).

The local medical advisory committee will participate in the development of the heart-demonstration program, and will consist of members of the public-health committee of the Newton Medical Club. These are Drs. George Bowers, Theodore Clark and Egon Kattwinkel, with Dr. Herbert G. Dunphy, president of the club, as *ex-officio* member. A committee from the Newton Dental Club is to be appointed.

MISCELLANY

SAFETY CONFERENCE

One session of the annual Safety Conference, held in April at the Statler Hotel, Boston, was sponsored by the Massachusetts Department of Public Health, Dr. Vlado A. Getting, commissioner, presiding.

Prevention of accidents was the keynote of the afternoon discussion, six speakers emphasizing safety points in their particular fields. Dr. Erich Lindemann, of the Massachusetts General Hospital, told of the "accident-proneness" of persons under emotional stress; Miss Frances Frazier, of the Harvard School of Public Health, urged assistance to the aged to prevent falls; and Dr. John F. Conlin spoke on "The Doctor — Preventive Medicine." Stephen Mahoney, of the Cambridge Recreation Department, stressed the necessity of regular inspection of playground equipment; Mrs. Frances Blair, president of the Massachusetts Parent-Teacher Association, spoke on the safety of children, and the concluding speaker, John Chandler, commissioner of agriculture, described the many accidents occurring on the farm.

BLUE SHIELD FINANCIAL REPORT

The Blue Shield plans of the country, according to a release from the national office in Chicago, recorded a total income of $48,445,245 during 1947. Of the sum so collected approximately 78 per cent was paid to physicians, 15 per cent went toward operating expenses, and the remainder was added to reserve accounts.

RESEARCH IN SKIN DISEASES

A new and intensive program of research in diseases of the skin was recently announced by Harvard Medical School and the Massachusetts General Hospital. The program, financed in part by the Rockefeller Foundation, will bring recent advances in physiology and biochemistry to bear in a search for new knowledge of skin diseases. It will be based on close co-operation between dermatologists and experts in general medicine.

To develop this new program, Dr. Chester North Frazier, head of the Department of Dermatology at the University of Texas, has been appointed Edward Wigglesworth Professor of Dermatology at Harvard University and chief of the Dermatology Service at the Massachusetts General Hospital. He will organize a new department of dermatology at the medical school and will lead the research and clinical program at the hospital.

CORRESPONDENCE

SUGGESTION FOR BETTER PHARMACEUTICAL METHODS

To the Editor: A serious problem confronts the medical profession. It is becoming more and more apparent that it is the policy of the drug manufacturers to release new drugs as tablets, capsules and ampoules. These are all high-priced dosage forms. The low-cost dosage forms like the powder, which can be used to fill prescriptions that need compounding, and the hypodermic tablet are not available.

A drug in point is methadon, which was taken from the Germans in World War II. A doctor attending a patient with a gall-bladder attack at night could give an injection of methadon from a hypodermic tablet and then dispense a few such tablets of methadon to be taken by mouth during the night. A hypodermic tablet would not cost more than three or four cents. However, since the tablet is not obtainable, an ampoule must be used for the injection, at a cost of sixteen cents. Then the doctor must have oral tablets of methadon to dispense. The hypodermic tablet can be used in two ways and — to make it more pleasant — is much cheaper. One must not forget that morphine sulfate has been used in the form of hypodermic tablets for many years, and certainly any of the new drugs can be used likewise.

The failure of the drug manufacturers to provide the powder form of drugs is even more serious. In the *U.S.P.* (13th edition) I have found that at least twenty of the newer drugs cannot be obtained in the powder form. Despite the publicity carried on by drughouses concerning the antihistaminics, the rank and file of physicians know of many failures with these drugs and would like to combine them in a prescription with ephedrine and aminophylline. If the antihistaminic failed, at least the ephedrine and the aminophylline would work in a case of asthma.

All physicians should write to the Council on Pharmacy and Chemistry of the American Medical Association urging that steps be taken to make all medicines available in powder form.

BENJAMIN L. YELLEN, M.D.
Brawley, California

BOOK REVIEWS

A History of Scientific English: The story of its evolution based on a study of biomedical terminology By Edmund Andrews, M.D. 8°, cloth, 342 pp., with 18 illustrations. New York: Richard R. Smith, 1947. $7.50.

Dr. Andrews, successful surgeon and erudite philologist, in this outstanding work has produced a history of the origin and transition of scientific language from its beginnings in historic times down to the present. Like some other philologists he believes that all language stems from an unknown ancestor of the prehistoric period. In successive chapters he considers Indo-European philology, semantics and the history of medical terminology. The following chapters discuss various historical aspects, including pre-Hellenic influences, the Aryan heritage, Greek, Latin (including dead or classical Latin), Arabic, French, German and English, divided into Anglo-Saxon, middle and modern. The final chapter deals with the future and advocates Basic English as a common scientific language. A good index concludes the text.

Although Dr. Andrews' book will appeal to comparatively few readers, it should be in all collections of medical and scientific history.

Emotional Maturity: The development and dynamics of personality. By Leon J. Saul, M.A., M.D. 8°, cloth, 338 pp. Philadelphia: J. B. Lippincott Company, 1947. $5.00.

The task of presenting psychodynamic understanding of human motivation that will reach a large and varied group is always a difficult one. In this book, the author presents his material in an extremely readable form. Although his orientation is psychoanalytic, he maintains a conscious oversimplification of the problem, sacrificing completeness and depth for clarity and schematization. He concerns himself with the main motive forces of behavior and personality, accentuating early training and environment but not entirely losing sight of the fundamental biologic drives. He gives considerable attention to the problem of neurosis, illustrating it with numerous well chosen cases.

This book is an excellent primer to the dynamics and development of personality couched in language designed for the layman. It also contains much of interest for those farther advanced in the field of psychiatry.

Medicine. By A. E. Clark-Kennedy, M.D., F.R.C.P. Volume 1. *The patient and his disease.* 8°, cloth, 383 pp. Baltimore: Williams and Wilkins Company, 1947. $6.00.

The author of this work, physician to the London Hospital and dean of its Medical School, rebels against the present-day textbook of medicine, rating it either as a compilation of second-hand facts or as a symposium of disconnected subjects by a panel of writers. This is a harsh and surely contestible evaluation. His own object is to give an account, based on his personal experience as practitioner and teacher, of the nature of the patient and to explain the meaning of his disease, correlating facts rather than enumerating them, and emphasizing the general principles underlying medicine as a whole. As a science medicine deals with the physical aspects of disease; as an art it handles all the complexities of the human mind and the many shades of human personality.

Some of the chapter headings in this volume suggest its scope and method: "Body and Mind"; "Symptoms and Signs"; "Heredity and Environment"; "Reactions of the Body and the Mind"; and "Nature of Disease." Each chapter has a comprehensive summary.

The following paragraph in the chapter on "The Nature of Disease" exemplify the author's style and thinking:

> The body of man and his mind, at least to some extent, are the product of organic evolution, the result of natural selection of variation in the struggle for existence. Every individual struggles for existence. His genetic endowment may handicap him from the start. Throughout his life he is exposed to all the dangers inherent in the physical world and to competition with other forms of life. There is never-ending competition between man and man. Danger lies in the power of man's will. Adverse factors in heredity and environment act on his body and disturb his mind. All tend to lessen his physical and mental efficiency, and produce pain and suffering. Many shorten his existence and may abruptly terminate his life. Without the power of adaptation the individual would not survive long and the human race would soon cease to maintain the dominant position which it occupies in the animal world.

It is a work well worth leisurely reading and study.

Radium Dosage: The Manchester System. Edited by W. J. Meredith, M.Sc., F.Inst.P. 8°, cloth, 124 pp., with 38 illustrations, 4 plates and 27 tables. Baltimore: Williams and Wilkins Company, 1947. $4.50

This publication is an extremely valuable compilation of papers that have appeared in recent years by members of the Holt Radium Institute at Manchester. A method of dosage measurement, correlated with a scheme of distribution giving homogeneity for planar and irregular moulds, cylinders and interstitial radium application, is described simply and lucidly. None of these methods, however, are applicable to the treatment of cancer of the cervix because of the great variation in size, shape and type of the parts and the tissues to be treated. A special chapter is devoted to this subject in which the types of radium applicators advised and the principles underlying their use are described.

Radium has had a much wider use in England than in this country, where, apparently, this therapy has been stymied by the ease with which x-ray dosage may be approximated and phased by the calculations necessary for accurate dosage when radium is employed. Very few clinicians have the type of mentality or the interest to wrestle with the theoretical physics involved in dosage measurement, but welcome data in readily applicable form.

Paterson and Parker, in England, and Quimby, in the United States, have done just that for radium dosage. They have reduced involved formulas to such simple terms that anyone with knowledge of arithmetic can apply them.

The first part of this monograph consists of the clinical aspects of the constituent papers rewritten to form a continuous whole. The purely physical aspects of the work are considered in the second part.

This book should be in the library of every radiologist and radiologic department.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Atlas of Bacteriology. By R. Cranston Low, M.D., F.R.C.P.E., F.R.S., member, Bacteriology Department, University of Edinburgh, and consulting physician, Skin Department, Royal Infirmary, Edinburgh; and T. C. Dodds, F.I.M.L.T., F.I.B.P., F.R.P.S., laboratory supervisor, Department of Pathology, University of Edinburgh, and lecturer to the Society of Radiographers (Fellowship Course), Scottish Branch. 8°, cloth, 168 pp., with 168 illustrations. Baltimore: Williams and Wilkins Company, 1947. $8.50.

The authors have produced an atlas primarily intended for undergraduate students to supplement class work and standard texts. All the plates except one are in color, and were made from actual color photographs and water-color drawings when it was found impossible to use photographs. Great care was taken to reproduce exact color tones, but unfortunately eight illustrations were reprinted too light in color and because of the shortage of paper could not be reprinted. Each figure shows the magnification stain and source of culture and notes any other pertinent facts. The color work is good, and the volume well published. The book should prove useful as a ready reference source.

Applied Medical Bacteriology. By Max S. Marshall, Ph.D. With the collaboration of Janet B. Gunnison, M.A., Alfred S. Lazarus, Ph.D., Elizabeth L. Morrison, M.A., and Marian C. Shevky, A.B., division of bacteriology, Medical Center of the University of California, San Francisco. 8°, cloth, 340 pp., with 10 illustrations and 12 tables. Philadelphia: Lea and Febiger, 1947. $4.50.

This practical manual has been written for the student, clinician and public-health worker interested in bacteriology

as applied to his problems. The early chapters have to do with the various technics. These are followed by chapters on viruses, yeasts and molds, biologic products and sanitation. The final chapter, consisting of over half the book, discusses the various diseases due to micro-organisms. These are arranged in alphabetical order, and describe the organism, specimens, microscopical examination, laboratory procedures and reports. The material is well arranged, the text well written, and the volume well published. A good index concludes the volume. An up-to-date list of biologic products and their makers is included.

Pharmacology and Experimental Therapeutics: A survey for 1941-1946. By Hamilton H. Anderson, Fumiko Murayama and Benedict E. Abreu. 8°, cloth, 368 pp. Berkeley and Los Angeles: University of California Press, 1947. $6.50.

In this survey the authors have arranged their material in an alphabetical form obviating the need for an index. The effects of drugs and therapeutic agents are briefly considered, and the references, on which the text is based, are made part of the text. The volume is well published and should prove useful as a reference source in medical libraries and valuable to all persons interested in pharmacology.

American Medical Research, Past and Present. By Richard H. Shryock, Ph.D., professor of history and lecturer in medical history, University of Pennsylvania, and acting director, American Council of Learned Societies. 8°, cloth, 350 pp. New York: The Commonwealth Fund, 1947. $2.50.

Dr. Shryock has written a history of American medical research from its beginning in the middle of the eighteenth century to the present time. The work is divided into twelve chapters, considering in order the formative period of British influence, 1750–1820; early support of research, 1860–1895; the era of private support by foundations and institutions, 1895–1940; research trends; research fields, public relations and public support. The last chapter analyzes the part Government agencies, federal, state and local, have taken in this field since 1940. The text is interesting and well written. Each chapter is documented with references to original sources. There is a good index, and the volume is well published. It should be in all medical, university and general libraries and in historical collections.

Teaching Psychotherapeutic Medicine: An experimental course for general physicians. By Walter Bauer, M.D., Douglas D. Bond, M.D., Henry W. Brosin, M.D., Donald W. Hastings, M.D., M. Ralph Kaufman, M.D., John M. Murray, M.D., Thomas A. C. Rennie, M.D., John Romano, M.D., and Harold G. Wolff, M.D. Edited by Helen L. Witmer, Ph.D. With an introductory chapter by Geddes Smith. 8°, cloth, 464 pp. New York: The Commonwealth Fund, 1947. $3.75.

This book is based on lectures and discussions of the pilot course in psychotherapy in general practice given at the University of Minnesota in 1946, covering a period of two weeks. Nine specialists took part in the presentation of papers and discussions, with illustrative case reports on backache and headache, psychoneuroses, anxiety neuroses, the care of veterans and life situation, emotions and disease. The early chapters deal with general orientation, history-taking, patient-physician relation and normal personality development. Twenty-five physicians took the course, and in addition to the lectures they treated by psychotherapy patients in the outpatient service who suffered from headache, backache, indigestion, vague and persistent pains, fatigue and nervousness. This teaching course was successful from a practical point of view. The volume is well published in every way and is recommended for all medical libraries and should prove valuable to the general practitioner.

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140 Million Patients. By Carl Malmberg. 12°, paper, 242 pp. New York: Reynal and Hitchcock, 1947. $2.75.

Mr. Malmberg was formerly information specialist for the United States Public Health Service and chief investigator for the United States Senate Subcommittee on Health and Education. In this volume he advocates the establishment of socialized medicine and the passage of the revised Wagner–Murray–Dingell Bill, introduced in Congress in May, 1947, as S 1320 and HR 3548. He discusses the subject in five pertinent sections: health inventory of the United States; the cost of sickness; the quality of American medical care; prescription for better health; and voluntary plans — "too little and too late." He concludes with a short chapter entitled, "140 Million Patients Can't Be Wrong."

The author believes that voluntary plans have reached their peak of service and that the Blue Cross has reached the saturation point although the increase in 1947 was 22 per cent over 1946, an increase of over five and a half million new enrollments.

He states that the Taft Bill (S 545, 80th Cong. First Session) is not constructive but is a delaying action to offset the Wagner–Murray–Dingell Bill.

In the statistical tables of infant and maternal mortality, general mortality and morbidity rates, only countries with a better showing than the United States are listed, those with poorer rates being ignored.

The paper-covered volume is well printed with a good type, on good paper. It should be in all public-health collections.

NOTICES

NEW YORK STATE SOCIETY OF ANESTHESIOLOGISTS

The third postgraduate assembly of the New York State Society of Anesthesiologists will be held at the Hotel New Yorker, New York City, on December 9 and 10.

AMERICAN COLLEGE OF SURGEONS

The thirty-fourth Clinical Congress of the American College of Surgeons will be held in Los Angeles, with headquarters at the Biltmore Hotel, from October 18 to 22. The program of scientific sessions on subjects in the fields of general surgery, eye, ear, nose, and throat surgery, gynecology and obstetrics, urology, and orthopedic, thoracic, plastic and neurologic surgery will be supplemented by operative clinics in hospitals in Los Angeles and vicinity by showings of operations by television and motion pictures, and by a four-day hospital-standardization conference for hospital personnel. There will also be extensive technical and scientific exhibits.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, July 8

Friday, July 9
*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.
12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

Tuesday, July 13
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

Wednesday, July 14
*12:00 m.–1:00 p.m. Clinical Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*Open to the medical profession.

June 28–July 23. Harvard Seminar on Health Education. Page 856, issue of June 10.

July 6-24. Students' International Clinical Congress. Page 455, issue of March 25.

July 12–17. First International Poliomyelitis Conference. Page 36, issue of January 1.

August 11–21. International Congress on Mental Health. Page 344, issue of March 4.

August 23–26. International Society of Hematology. Page 419, issue of March 18.

August 26–28. American Association of Blood Banks. Page 420, issue of March 18.

September 7–11. American Congress of Physical Medicine. Page 582, issue of April 15.

September 13–15. American Academy of Pediatrics. Olympic Hotel, Seattle, Washington.

September 16–18. Vermont State Medical Society. Annual Meeting, Burlington.

September 20–23. American Hospital Association. Page 310, issue of February 26.

(*Notices concluded on page xiii*)